chain nodes :

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Uploading C:\Program Files\Stnexp\Queries\10580610-registry-product-4.str
```

```
7 8 9 10 11 12 14 15 16 17 18 19 20 21 22 23 24 25 26 27
ring nodes :
1 2 3 4 5 6
chain bonds :
1-25 2-24 3-23 4-22 5-7 6-26 7-8 8-9 9-10 9-19 10-11 11-12 11-14 12-18
12-27 15-17 15-16 15-27 19-20 19-21
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-25 \quad 2-24 \quad 3-23 \quad 4-22 \quad 6-26 \quad 9-10 \quad 9-19 \quad 10-11 \quad 11-12 \quad 12-18 \quad 12-27 \quad 15-17 \quad 15-16
15-27 19-20 19-21
exact bonds :
5-7 7-8 8-9 11-14
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :
```

Match level: 1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS 22:CLASS 22:CLASS 22:CLASS 22:CLASS 25:CLASS 25:CLASS 26:CLASS 27:Atom Generic attributes:

27: Saturation : Saturated

Number of Hetero Atoms : Exactly 1
Type of Ring System : Polycyclic

L32 STRUCTURE UPLOADED

L32 STRUCTURE UPLOADED
L34 83 S L32 SSS FULL SUB=L18

FILE 'CAPLUS' ENTERED AT 10:01:13 ON 05 MAY 2008

L35 811 S L34

L36 111 S L35 AND SPN/RL

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V
     L36 ANSWER 1 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
           Radioimaging moieties coupled to peptidase-binding moieties for imaging
    tissues and organs that express peptidases
     L36 ANSWER 2 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
           Methods and compositions of gene delivery to epithelial cells through
bile
    acid peptide conjugate delivery agents for systemic and local therapy
     L36 ANSWER 3 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
           Preparation of pyrrolopyrimidines having Mnk1/Mnk2 inhibiting activity
     L36 ANSWER 4 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
           Preparation of 1-heterocyclylamino-2-hydroxy-3-amino-@-arylalkanes
    as renin inhibitors for treating hypertension and other renin-mediated
    diseases
     L36 ANSWER 5 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
ΤI
           6-(Aminoalkyl)indazoles as renin inhibitors and their preparation,
    pharmaceutical compositions and use in the treatment of diseases
    associated with renin activity
V
     L36 ANSWER 6 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
           Acylpiperidine compounds as renin inhibitors and their preparation,
    pharmaceutical compositions and use in the treatment of diseases
    associated with aspartic protease activity
V
     L36 ANSWER 7 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
ΤI
           Piperidinyl pyrrolidinyl methanone compounds as renin inhibitors and
their
    preparation, pharmaceutical compositions and use in the treatment of
    diseases associated with aspartic protease activity
```

L36 ANSWER 8 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

pharmaceutical compositions

Thienopyrimidines having Mnk1/Mnk2 inhibiting activity for

- √ L36 ANSWER 9 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI V Piperidines and morpholines as renin inhibitors and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with renin activity
- √ L36 ANSWER 10 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI √ Preparation of substituted thiazolopyridines as PPAR modulators
- √ L36 ANSWER 11 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI √ Preparation of substituted thiazolyl tetrahydroisoquinolines as PPAR modulators
- √ L36 ANSWER 12 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI V Spiro imidazole derivatives as PPAR modulators and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with PPAR activity.
- √ L36 ANSWER 13 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI $\sqrt{}$ Oxazoles and thiazoles as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
- √ L36 ANSWER 14 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI √ Oxazoles and thiazoles as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
- √ L36 ANSWER 15 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI √ Oxazoles and thiazoles as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
- √ L36 ANSWER 16 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI $\sqrt{}$ Combination of a dipeptidyl peptidase-4 inhibitor and an antihypertensive
 - agent for the treatment of diabetes and hypertension
- √ L36 ANSWER 17 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2007:397799 CAPLUS Fuil-text
- DN 147:212296
- TI Improved process for preparation of trandolapril
- IN Dattatraya, Patil Vishvas; Sharadrao, Varangaonkar Aniruddha
- PA Torrent Pharmaceuticals Ltd., India

SO Indian Pat. Appl., 19pp.

CODEN: INXXBQ

Patent DT LA English

FAN.CNT 1

I	PATENT NO.	KIND	V	DATE		APPLICATION NO.	DATE
-							
	IN 2004KO00355 IN 2004-KO355	A		0825 10625	IN	2004-K0355	20040625

CASREACT 147:212296 OS

The invention discloses an improved process for the preparation of AB (2S, 3aR, 7aS)-1-[N-[(S)-1-carbethoxy-3-phenylpropy1]-L-alanyl]hexahydro-2indolinecarboxylic acid, i.e., trandolapril. Key steps in the process include treating Me 3-chloro-N-acetylalanine with 1- pyrrolidinocyclohexene, followed by hydrolysis with 2N HCl and reductive cyclization over Pt/C to obtain 2β, 3aβ, 7aα-1H- octahydroindole-2-carboxylic acid hydrochloride. The N-benzoyl

derivative was resolved via formation of the L- α -phenylethylamine salt.

87679-37-6P, Trandolapril

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(improved process for preparation of trandolapril)

87679-37-6 CAPLUS RN

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

98677-37-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (improved process for preparation of trandolapril)

98677-37-3 CAPLUS RN

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S, 3aR, 7aS) - (CA INDEX NAME)

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V
    L36 ANSWER 18 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
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AN 2007:388837 CAPLUS Full-text

147:541727 DN

Process for the preparation of trandolapril and intermediates thereof

IN Joshi, Narendra Shriram; Bhirud, Shekhar Bhaskar; Ramam, Buddhavarapu

Pattabhi; Bodkhe, Arjun Rajaram

PA Glenmark Pharmaceuticals Limited, India

SO Indian Pat. Appl., 31pp.

CODEN: INXXBQ Patent

LA English

FAN.CNT 1

PATENT NO.

KIND DATE APPLICATION NO. DATE ____ _____ √ 20060728 IN 2004-MU1060 PI IN 2004MU01060 20041007 PRAI IN 2004-MU1060 20041007

OS CASREACT 147:541727

GI

L36 ANSWER 19 OF 111 CAPLUS COPYRIGHT 2008 ACS on

STN AN 2007:300486 CAPLUS Full-text DN 147:522095

TI Process for the preparation of trans-octahydro-1H-indole-2-carboxylic acid

IN Debashish, Datta; Jagannath, Wani Mukesh

Lupin Ltd., India PA

Indian Pat. Appl., 37pp. SO CODEN: INXXBO

DT Patent

LA English FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE PI IN 2003MU01033 20060120 IN 2003-MU1033 20031003 PRAI IN 2003-MU1033 20031003

OS CASREACT 147:522095

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

- The invention relates to a process for the preparation of octahydroindole-2carboxylic acid of formula I, wherein the ring junction is trans, including enantiomers, esters, and salts thereof, and more specifically (2S, 3aR, 7aS)octahydro-1H-indole-2-carboxylic acid (II) and esters and salts thereof. Compound II is a valuable intermediate in the synthesis of the angiotensin converting enzyme (ACE) inhibitor trandolapril. The process of the invention avoids the use of expensive, hazardous, toxic, and corrosive chems., very low temps., and gives about 50% of the trans-isomer, making the process of the invention more com. attractive than prior art. The target compds. may be prepared according to the process of the invention as shown by the following example. Rhodium-catalyzed hydrogenation of the hydrochloride of imino acid III in water under alkaline conditions gave about 1:1 mixture of the transand cis-isomers of I. Fractional crystallization of the mixture from methanol resulted in the isolation of II and its enantiomer. Acetylation followed by diastereomeric salt formation with cinchonidine and acidification gave IV with 99.7% optical purity. Compound IV underwent deacetylation with hydrochloric acid to give II, which may be used to prepare trandolapril (V) in a single step.
- IT 87679-37-6P, Trandolapril

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(target compound; process for preparation of trans-octahydro-1H-indole-2-carboxylic acid)

RN 87679-37-6 CAPLUS

1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenvlpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

- √ L36 ANSWER 20 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI V Nitric oxide enhancing angiotensin II antagonist compounds, and their preparation, compositions, and methods of use
- √ L36 ANSWER 21 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2007:37921 CAPLUS Full-text
- DN 146:143003
- TI Process for the preparation of trandolapril from N-[1-(5)-ethoxycarbonyl-3phenylpropyl]-L-alanine N-carboxyanhydride and trans-octahydro-1H-indole-2carboxylic acid.
- IN Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra; Phull, Manjinder

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Singh; Sawant, Ashwini; Birari, Dilip Ramdas
PA
    Cipla Limited, India; Curtis, Philip, Anthony
SO
    PCT Int. Appl., 20 pp.
    CODEN: PIXXD2
    Patent
    English
LA
FAN.CNT 1
                      KIND DATE
    PATENT NO.
                                         APPLICATION NO.
                                                               DATE
                       A2
                             20070111
                                        WO 2006-GB2496
                                                               20060705
    WO 2007003947
                       A3 20070531
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
            KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
            MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU,
            SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG,
            US, UZ, VC, VN, ZA, ZM, ZW
        RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
            IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
            CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
            GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
    IN 2005MU00793
                        A
                             20070601
                                         IN 2005-MU793
                                                                20050705
    CA 2614099
                        A1
                              20070111
                                         CA 2006-2614099
                                                                20060705
    EP 1899300
                                        EP 2006-755717
                        A2
                             20080319
                                                                20060705
        R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
            IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
                      A
                              √ 20050705
PRAI IN 2005-MU793
    WO 2006-GB2496
                       W
                              20060705
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- √ L36 ANSWER 22 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

L36 ANSWER 23 OF 111 CAPLUS COPYRIGHT 2008 ACS on

STI	Ŋ				
AN	2006:1339720 CAPI	US Ful.	l-text		
DN	146:82189				
TI	Preparation of L-t	hreonin	e derivative	s with high therapeuti	c index
IN	Chandran, V. Ravi				
PA	USA				
so	U.S. Pat. Appl. Pt CODEN: USXXCO	ıbl., 60 ₁	pp., Conti	n-part of U.S. Ser. No	. 343,557.
DT	Patent				
LA	English				
FAN.	CNT 3				
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20060287244	A1	20061221	US 2006-442027	20060526
	WO 2005046575	A2	20050526	WO 2004-US24901	20040729
	WO 2005046575	A3	20071004		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, AP, EA, EP, OA

US 2006-343557

20060130

US 20060241017 A1 20061026 PRAI US 2003-491331P P 20030729 WO 2004-US24901 20040729 A2

US 2006-343557 A2 20060130

The invention is directed to novel therapeutic compds. comprised of an L-AB threonine bonded to a medicament or drug having a hydroxy, amino, carboxy or acylating function. These high-therapeutic index derivs, have the same utility as the drug from which they are made and they have enhanced pharmacol. and pharmaceutical properties, with the addnl. advantage of separating various enantiomeric and diastereomeric drugs into their individual isomers. The examples describe the synthesis and activities of L-threonine derivs. of (\pm) and (+)-(S)-ibuprofen, (\pm) - and (+)-(S)-ketoprofen, (-)-(S)-ketorolac, aspirin, and fenofibric acid. The synthesis and activity of several L-serine and L-hydroxyproline analogs were also described. Thus, the hydrochloride of (+)-(S)-ibuprofen ester of L-threonine was prepared, and its free base examined for analgesic, gastric mucosal irritation, toxicity, and pharmacokinetic properties.

917472-72-19

TT

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of L-threonine derivs, with high therapeutic index) RN 917472-72-1 CAPLUS

L-Threonine, ester with (2S, 3aR, 7aS)-1-[(2S)-2-[[(1S)-1-carboxy-3-CN phenylpropyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (CA INDEX NAME)

CM 1

CRN 87679-71-8 CMF C22 H30 N2 O5

CM 2

CRN 72-19-5 CMF C4 H9 N O3

Absolute stereochemistry.

- IT 87679-71-8, Trandolaprilat
 - RL: RCT (Reactant); RACT (Reactant or reagent)
 - (preparation of L-threonine derivs. with high therapeutic index)
- RN 87679-71-8 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S, 3aR, 7aS)- (CA INDEX NAME)

- √ L36 ANSWER 24 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI $\sqrt{}$ Preparation of pyrazole compounds as hepatic glycogen phosphorylase inhibitors and therapeutic agents for diabetes
 - √ L36 ANSWER 25 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI √ Preparation of 4-biarylyl-1-phenylazetidin-2-ones for the treatment of hypercholesterolemia
- √ L36 ANSWER 26 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2006:1222092 CAPLUS Full-text
- DN 146:7821
- TI Process for the preparation of (2S,3aR,7aS)-octahydroindole-2-carboxylates and their conversion to trandolapril
- IN Akhtar, Haider; Ramesh, Babu Potluri; Venkata, Subhramanian

Hariharakrishnan; Hari, Prassad Kodali

- PA Sochinaz SA, Switz.
- Eur. Pat. Appl., 19pp. SO CODEN: EPXXDW
- Patent
- T. D English

FAN.		1																
	PA'	TENT	NO.			KIN	D	DATE			APPL	ICAT	ION	NO.		D.	ATE	
							-											
PI	EP	1724	260			A1		√	2006	1122		EP 2	005-	7606	0		2	0050506
	EP	1724	260			B1		2008	0220									
		R:	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HU,	IE,
			IS,	IT,	LI,	LT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	SK,	TR,	AL,	BA,
			HR,	LV,	MK,	YU												
	AT	3867	18			T		2008	0315		AT 2	005-	7606	0		2	0050	506
PRAI	EP	2005	-760	60		A		2005	0506									
os	CA:	SREAC	T 14	6:78	21;	MARP.	AT 1	146:7	821									

AB A process for preparation of benzyl (2S, 3aR, 7aS)-octahydroindole-2-carboxylate hydrohalide (I; X, Y = H, halo, alkyl, alkoxy), and its conversion to trandolapril comprises (a) reaction of Me β-hydroxyalaninate hydrochloride with an acylating agent in a nonpolar solvent to give a diacylated derivative, (b) reaction of the latter with a cyclohexanone enamine to give Me N-acyl-β-(2-oxocyclohexyl)alaninate, (c) hydrolytic cyclization to give an indole, (d) hydrogenation to a perhydroindole derivative, (e) esterification with a benzyl alc. followed by conversion of the benzyl ester arylsulfonate to the hydrohalide I, (f) resolution and conversion to a benzyl (2S, 3aR, 7aS)octahydroindole-2-carboxylate hydrohalide, and (q) coupling with ECPPA (N-[(1ethoxycarbonvl)-3- phenylpropyll-(S)-alanine) acid chloride hydrochloride and debenzylating hydrogenolysis.

L36 ANSWER 27 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

ΤI 4-Biarylyl-1-phenylazetidin-2-one glucuronide derivatives for hypercholesterolemia

L36 ANSWER 28 OF 111 CAPLUS COPYRIGHT 2008 ACS on

STN

- 2006:1124123 CAPLUS Full-text
- DN 145:455276
- ΤI Preparation of amino acid derivatives with high therapeutic index
- IN Chandran, V. Ravi
- PA IISA

SO U.S. Pat. Appl. Publ., 139pp. CODEN: USXXCO

DT Patent

LA English FAN.CNT 3

P

		TENT I				KIN		DATE			APPL						ATE	
I		2006				A1		2006			US 2						0060	
	WO	2005	0465	75		A2		2005	0526		WO 2	004-1	US24	901		2	0040	729
	WO	2005	0465	75		A3		2007	1004									
		W:	AE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,
			CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
			GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,
			LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,
								PL,										
			TJ.	TM.	TN.	TR.	TT.	TZ,	UA.	UG.	US.	UZ.	VC.	VN.	YU.	ZA.	ZM.	ZW
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			AZ,	BY,	KG,	KZ,	MD,	RU,	TJ,	TM.	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,
			EE,	ES.	FI.	FR.	GB,	GR,	HU,	IE,	IT,	LU,	MC,	NL,	PL,	PT.	RO,	SE,
			SI,	SK,	TR.	BF,	BJ,	CF,	CG,	CI,	CM,	GA,	GN,	GO,	GW,	ML,	MR,	NE.
								EP,										
	US	2006	0287	244		A1		2006	1221		US 2	006-	4420	27		2	0060	526
	WO	2007	0897	45		A2		2007	0809		WO 2	007-1	JS24	75		2	0070	129
		W:	AE,	AG,	AL,	AM.		AU,								BZ.	CA.	CH.
								DE,										
								HR,										
								LK,										
			MN.	MW.	MX,	MY,	MZ,	NA.	NG,	NI,	NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,
			RS,	RU,	SC.	SD,	SE,	SG,	SK,	SL,	SM,	SV,	SY,	TJ,	TM.	TN.	TR.	TT.
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		RW:	AT.	BE,	BG,	CH,	CY,	CZ,	DE.	DK.	EE,	ES,	FI,	FR,	GB,	GR,	HU,	IE,
								MC,										
								GN,										
								NA,										
						RU,												
DAT	TTC	2002							0720									

PRAI US 2003-491331P P 20030729 WO 2004-US24901 A2 20040729

US 2006-343557 A2 20060130

- AB The invention is directed to novel therapeutic compds. comprised of an amino acid bonded to a medicament or drug having a hydroxy, amino, carboxy or acylating function. These high-therapeutic index derive. have the same utility as the drug from which they are made and they have enhanced pharmacol. and pharmaceutical properties. The examples describe the synthesis and activities of amino acid derive. of propofol, ibuprofen, ketoprofen, ketorolac, aspirin, acetaminophen, cyclosporin A, valproic acid, clopidogrel, damazol, benzapril, enalapril, and fenofibric acid. Thus, (±)-ibuprofen esters of L-serine, L-threonine, and L-hydroxyproline were prepared and examined for analgesic, gastric mucosal irritation, toxicity, and pharmacokinetic properties.
- IT 87679-71-8, Trandolaprilat

RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(preparation of amino acid derivs. with high therapeutic index)

RN 87679-71-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-carboxy-3-phenylpropy1]amino]-1-oxopropy1]octahydro-, (2S, 3aR, 7aS)- (CA INDEX NAME)

L36 ANSWER 29 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

TI $\,$ Organic nitric oxide enhancing salts of angiotensin II antagonists, compositions and methods of use

√ L36 ANSWER 30 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

TI $\sqrt{}$ Preparation of nitric oxide enhancing diuretic compounds, compositions and

methods of use

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√ L36 ANSWER 31 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
```

AN 2006:818063 CAPLUS Full-text

DN 145:211348

II Improved process for preparation of highly pure trandolapril

IN Singh, Girij Pal; Wani, Mukesh Jagannath; Lande, Hemraj Mahadeorao; Jain, Adinath Murlidhar

PA Lupin Limited, India

SO PCT Int. Appl., 34pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1																			
	PATE	NT I	.OV			KIND DATE			APPLICATION NO.				DATE						
															-				
PI	WO 2	006	0853	32		A1		2006	0817		WO 2	005-	IN30	1		7		20050906	
		W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,	
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			GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KM,	KP,	KR,	KZ,	
			LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	
			NG,	NΙ,	NO,	ΝZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	
			SL,	SM,	SY,	ΤJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	
			ZA,	ZM,	ZW														
		RW:	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FΙ,	FR,	GB,	GR,	HU,	IE,	
			IS,	ΙT,	LT,	LU,	LV,	MC,	NL,	PL,	PΤ,	RO,	SE,	SI,	SK,	TR,	BF,	BJ,	
			CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG,	BW,	GH,	
			GM,	KE,	LS,	MW,	ΜZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,	

KG, KZ, MD, RU, TJ, TM IN 2005MU00155 A 20060908 IN 2005-MU155 20050214 AU 2005327440 20060817 AU 2005-327440 A1 EP 1866327 A1 20071219 EP 2005-823818 20050906 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR PRAI IN 2005-MU155 Α 20050214 WO 2005-IN301 W 20050906

OS CASREACT 145:211348

AB

Highly pure trandolapril was prepared by acylation of benzyl trans-(2S, 3aR, 7aS)-octahydro-1H-indolecarboxylate [(2S, 3aR, 7a)-I] with N-[1-(S)ethoxycarbonyl-3-phenylpropyl]-L-alanine N-carboxyanhydride, followed by crystallization from appropriate solvents. (2S, 3aR, 7a)-I was prepared by (1) crystallization of a mixture of racemic I tosylates (2S, 3aR, 7aS and 2R, 3aS, 7aR) to enrich the purity to >99% from a mixture containing the cis diastereomers up to 6 %, (2) optical resolution of the racemic mixture of (2S, 3aR, 7aS) - and (2R, 3aS, 7aR) -I with (-)-dibenzoyl-L-tartaric acid monohydrate, (3) reaction of the tartrate salt with N-[1-(S)- ethoxycarbonyl-3-phenylpropyl]-L-alanine N-carboxyanhydride to give trandolapril benzyl ester, and crystallization of crude trandolapril. Trandolapril obtained by this process had HPLC purity 99.94% and a characteristic X-ray powder diffraction pattern.

87679-37-6P, Trandolapril

RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (X-ray powder diffraction; preparation of highly pure trandolapril)

RM 87679-37-6 CAPLUS

CN 1H-Indole-2-carboxvlic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonvl)-3phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

98677-37-3E

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of highly pure trandolapril)

RN 98677-37-3 CAPLUS

1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-CN phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S, 3aR, 7aS) - (CA INDEX NAME)

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

 $\sqrt{}$ L36 ANSWER 32 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN TI $\sqrt{}$ Hydroxylated nebivolol metabolites for treating and/or preventing vascular diseases

 $\sqrt{}$ L36 ANSWER 33 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN TI $\sqrt{}$ 1-Acylamino-2-hydroxy-3-amino-w-arylalkanes as renin inhibitors and their

preparation, pharmaceutical compositions and their use for treatment of hypertension $% \left(1\right) =\left(1\right) +\left(1\right$

√ L36 ANSWER 34 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Preparation of 4[(benzimidazoly1/pyrazoly1/triazoly1)methoxy]phenoxyaceti
c acids as PPAR modulators

 $\sqrt{}$ L36 ANSWER 35 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN TI $\sqrt{}$ Preparation of pyrazolopyrimidines as inhibitors of kinase activity

V L36 ANSWER 36 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Diuretic compounds comprising heterocyclic nitric oxide donor groups, compositions and methods of use

m V L36 ANSWER 37 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN TI m V Nitrosated and nitrosylated compounds, compositions, and methods for

√ L36 ANSWER 38 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2006:341506 CAPLUS Full-text

DN 144:350983

TI Process for the preparation of (2S,3aR,7aS)-perhydroindole-2-carboxylic acid intermediate in synthesis of trandolapril

IN Joshi, Narendra Shriram; Bhirud, Shekhar Bhaskar; Ramam, Buddhavarapu Pattabhi; Bodkhe, Arjun Rajaram

PA Glenmark Pharmaceuticals Limited, India

SO U.S. Pat. Appl. Publ., 10 pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20060079698	A1	20060413	US 2005-245871	20051007
PRAI	US 2004-616934P	P	√ 2004100°	7	
	US 2004-616959P	P	20041007		
os	CASREACT 144:350983;	MARPA	T 144:350983		

AB Trandolapril intermediate (2S, 3aR, 7aS)-perhydroindole-2-carboxylic acid was prepared by a process which comprises esterification of (3aR, 7aS)-perhydroindole-2-carboxylic acid with an alc. in the presence of an acid, reacting the acid addition salt with a base and then dibenzoyl-1-tartaric acid or di-p-toluoyl-1-tartaric acid and at least one alc., followed by addition of a second base and hydrolysis. (2S, 3aR, 7aS)-perhydroindole-2-carboxylic acid prepared by this method was used to prepare trandolapril.

IT 87679-37-6P, Trandolapril

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of perhydroindolecarboxylic acid intermediate in synthesis of trandolapril)

RN 87679-37-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

 $\sqrt{}$ L36 ANSWER 39 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN TI $\sqrt{}$ Preparation of bicyclic anilide spirolactam cgrp receptor antagonists

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V L36 ANSWER 40 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI V Preparation of tricyclic anilide spirohydantoin CGRP receptor antagonists.
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V
     L36 ANSWER 41 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
AN
     2006:119252 CAPLUS Full-text
DN
    144:171268
ΤI
    Preparation of trandolapril
     Reddy, Pratap Padi; Chitre, Saurabh Shashikant; Polavarapu, Srinivas;
IN
     Vakamudi Sri Naga Venkata Laxmi, Varaprasad
     Dr. Reddy's Laboratories Ltd., India: Dr. Reddy's Laboratories, Inc.
PA
     PCT Int. Appl., 21 pp.
SO
     CODEN: PIXXD2
DT
     Patent
    English
LA
FAN.CNT 1
     PATENT NO.
                        KIND
                               DATE
                                           APPLICATION NO.
                                                                  DATE
PΙ
    WO 2006014916
                         A2
                               20060209
                                          WO 2005-US26423
                                                                   20050726
     WO 2006014916
                         A3
                               20060803
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
            NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
             SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
             ZA, ZM, ZW
        RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
            GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
     IN 2007CN00572
                         A
                               20070824
                                           IN 2007-CN572
                                                                 20070208
                               V
PRAI US 2004-591035P
                         Р
                                   20040726
     US 2004-607839P
                         P
                               20040908
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OS CASREACT 144:171268
AB The invention relates to a process fo

WO 2005-US26423

The invention relates to a process for preparing trandolaprii, $(2S, 3aR, 7aS)-1-(R)-(S)-1-carbethoxy-3-phenylpropyl]-L-alanyl]hexahydro-2- indolinecarboxylic acid, and intermediates formed in the process. Thus, <math>(\pm)$ -benzyl octahydro-2-indolecarboxylate hydrochloride was treated with N-[(S)-1-carbethoxy-3-phenylpropyl]-L-alanie in CH2Cl2 in the presence of hydroxybenzotriazole and dicyclohexylcarbodiimide at $20-25^\circ\mathrm{C}$ for 3 h. Hydrogenation over 10% Pd on charcoal and workup, including recrystn., afforded trandolapril.

20050726

V L36 ANSWER 42 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

TI $\sqrt{}$ Thiazole compounds as PPAR modulators, their preparation, pharmaceutical

- √ L36 ANSWER 43 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI $\sqrt{}$ Oxazole compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
- √ L36 ANSWER 44 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI V Triaryl compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
- √ L36 ANSWER 45 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI $\sqrt{}$ Isoxazole compounds as PPAR modulators, their preparation, pharmaceutical

compositions, and use in therapy

- √ L36 ANSWER 46 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI $\sqrt{}$ Combination of (S)-amlodipine and an ACE inhibitor for reducing hypertension
- √ L36 ANSWER 47 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI $\sqrt{}$ Preparation of diacylglycerol acyltransferase (DGAT1) inhibitors as anorectics.
- √ L36 ANSWER 48 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI √ Nitric oxide-releasing pyruvate compounds, compositions and methods for treating cardiovascular and other diseases

V	L36 ANSWER 49 OF	111 CAPLUS	COPYRIGHT 2008 ACS on STN -	INSTANT
	PATENT NO.	KIND DATE	APPLICATION NO.	DATE
PI	WO 2005054194	A1 2005	0616 WO 2004-EP13377	20041125
	US 20070225505	A1 200°	70927 US 2007-580610	20070212
PRAI	EP 2003-257417	A 2000	31125	
	WO 2004-EP13377	W 200	11125	

AΒ

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V
      L36 ANSWER 50 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
AN
     2005:493585 CAPLUS Full-text
DN
     143:32341
TΤ
     Method for producing {N-[1-(S)-carbalkoxy-3-phenylpropyl]-S-alanyl-2S,
     3aR, 7aS-octahydroindol-2-carboxylic acid} compounds especially
     trandolapril via their racemic salts
IN
     Pogutter, Mirko; Rudolf, Felix; Bichsel, Hans-Ulrich; Bader, Thomas
PA
     Azad Pharmaceuticals Ingredients A.-G., Switz.
SO
     PCT Int. Appl., 37 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     German
FAN.CNT 1
P
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	PATENT NO.			KIND DATE			APPLICATION NO.					DATE						
PI	WO	2005	0519	09		A1		2005	0609		WO 2	004-	CH68	8				20041115
		W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,
			CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
			GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	ΚP,	KR,	ΚZ,	LC,
			LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NA,	NI,
			NO,	ΝZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,
			ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UΖ,	VC,	VN,	YU,	ZA,	ZM,	ZW
		RW:						MW,										
			ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ΤJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,
			EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	IS,	IT,	LU,	MC,	NL,	PL,	PT,	RO,
							BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,
					TD,													
	EP	1689																
		R:						ES,								SE,	MC,	PT,
					FΙ,			TR,										
		2007				T		2007									0041	
		2006						2007									0060	
		2007						2007			US 2	007-	5806	38		20	0070	208
PRAI	CH	2003	-203	3		A		2003	1128									

WO 2004-CH688 W 20041115
The invention relates to a method for producing optionally substituted {N-[1-(S)-carbalkoxy-3-phenylpropyl]-S-alanyl-2S, 3aR, 7aS-octahydroindol-2-carboxylic acid) and the pharmaceutically acceptable salts thereof. To this end, a racemic mixture of optionally substituted trans-octahydroindol-2-carboxylic acid is reacted with the N-carboxyanhydride of (N-[1-(S)-alkoxycarbonyl-3-phenylpropyl]-L-alanine), which is optionally substituted on the Ph ring, in an appropriate inert solvent, and the obtained optionally substituted (N-[1-(S)-carbakkoxy-3-phenylpropyl]-S-alanyl-2S, 3aR, 7aS-octahydroindol-2-carboxylic acid), preferably trandolapril, is subsequently isolated, as well as polymorphous forms A and B of trandolapril.

- V L36 ANSWER 51 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN ΤI Preparation of nitrosated glutamic acid compounds for use in pharmaceutical compositions V L36 ANSWER 52 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN Preparation of biphenyl or phenylheterocyclyl moiety-containing esters as inhibitors of microsomal triglyceride transfer protein L36 ANSWER 53 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN 2'-Benzothiazolylthioesters of N-substituted alpha amino acids: versatile intermediates for synthesis of ACE inhibitors Synthetic Communications (2005), 35(2), 243-248 SO V L36 ANSWER 54 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN Nitrosated and nitrosylated cardiovascular compounds, their compositions, and use L36 ANSWER 55 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN ΤТ Preparation of benzodiazepine derivatives as CGRP receptor antagonists $\sqrt{}$ L36 ANSWER 56 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN ΤТ Preparation of phosphorus-containing rapamycin derivatives for use in pharmaceutical compositions as immunosuppressive and anticancer agents L36 ANSWER 57 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN Preparation of 5-substituted 2H-pyrazole-3-carboxylic acid derivatives as
- $\sqrt{}$ L36 ANSWER 58 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN TI $\sqrt{}$ Preparation of α -amino acid benzothiazolylthio esters as intermediates for manufacture of ACE inhibitors.

dyslipidemia and related diseases

agonists for the RUP25 nicotinic acid receptor for the treatment of

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L36 ANSWER 59 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
          Preparation of benzodiazepine CGRP receptor antagonists
     L36 ANSWER 60 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TΙ
         Enalapril-nitroxy derivatives and related compounds as ace inhibitors
for
     the treatment of cardiovascular diseases
     PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 2004110432 A1 20041223 WO 2004-EP51089 20040611
PRAI EP 2003-101796 A 20030619
                             √ 20040611
    WO 2004-EP51089
                       TAT
V
    L36 ANSWER 61 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI Process for the preparation of enalapril maleate and related compounds
    having ACE inhibitory action
IN
    Jenko, Branko
PA
    Lek Pharmaceuticals D.D., Slovenia
SO PCT Int. Appl., 18 pp.
    CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
     PATENT NO.
               KIND DATE APPLICATION NO. DATE
                                          _____
                             20041125 WO 2004-SI21 √ 20040507
   WO 2004101515
                       A1
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
            TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
            AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
            EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
            SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE,
            SN, TD, TG
     SI 21507
                            20041231 SI 2003-123
20060301 EP 2004-731808
                                                                20030516
     EP 1628956
                        A1
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
US 20070072919 A1 20070329 US 2006-556986
PRAI SI 2003-123 A 20030516
WO 2004-S121 W 20040507
                                                               20060929
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- 141:366125 DN
- Preparation of trandolapril from diastereomeric salt of benzyl TI (2S, 3aR, 7aS)-hexahvdro-2-indolinecarboxvlate
- TN Shimamura, Hiroshi
- Ohara Pharmaceutical Co., Ltd., Japan PA
- SO Jpn. Kokai Tokkyo Koho, 8 pp.
- CODEN: JKXXAF
- Patent
- LA Japanese
- FAN.CNT 1

	PATENT NO.	KIND	DATE API	PLICATION NO.	DATE
PI	JP 2004307340	A	√ 20041104	JP 2003-73056	20030318
DD 3 T	TD 0000 00010	_	00000000		

- PRAI JP 2003-37749 A 20030217 Trandolapril (I) is prepared by amidation of benzyl (2S, 3aR, 7aS)-hexahydro-2indolinecarboxylate (II) salt with optically active 10-camphorsulfonic acid,
 - with N-[1-(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanine or its Ncarboxyanhydride (III) in tertiary amine-containing solvent, followed by hydrogenolysis of the resulting amide benzyl ester. Thus, II.(1R)-(-)-10camphorsulfonate was amidated with III in DMF in the presence of Et3N, then hydrogenated over Pd/C to give I with 82% total yield.
 - V L36 ANSWER 63 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- Preparation of azole compounds as PTP1B inhibitors
- L36 ANSWER 64 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- ΤТ Evaluation of adsorption and penetration of angiotensin converting
- enzyme inhibitor, trandolapril, and its active metabolite, trandolaprilate, to the dialysis membrane
- ΑU Zaitsu, Kiyoshi; Hamase, Kenji; Hayashi, Hiromi; Nagayasu, Reiko; Fukuda, Hiroko; Tomita, Tatsunosuke; Morikawa, Akiko
- CS Graduate School of Pharmaceutical Sciences, Kyushu University, Japan
- SO Igaku to Yakugaku (2004), 51(6), 843-849 CODEN: IGYAEI; ISSN: 0389-3898
 - L36 ANSWER 65 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN CHECKED DOC
- ΤI Novel crystalline forms of trandolapril
- V L36 ANSWER 66 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- AN 2004:633914 CAPLUS Full-text
- DN 141:140316
- Process for producing intermediate for trandolapril by esterification of racemic (2S, 3aR, 7aS)-hexahydroindoline-2-carboxylic acid with benzyl alcohol and optical resolution
- TN Shimamura, Hiroshi; Nakata, Yoshitaka

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PA Ohara Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 15 pp.
    CODEN: PIXXD2
DT Patent
T.A
   Japanese
FAN.CNT 1
    PATENT NO. KIND DATE APPLICATION NO. DATE
                      ----
PI WO 2004065368 A1 √ 20040805 WO 2004-JP374 20040119
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
           CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
           GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
           LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ
V
    L36 ANSWER 67 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:605707 CAPLUS Full-text
DN 141:117164
TI Preparation of (2S, 3aR, 7aS)-1-[(S)-N-[(S)-1-ethoxycarbonyl-3-
    phenylpropyllalanyllhexahydro-2-indolinecarbon acid benzyl ester as an
    antihypertensive agent
IN Shimamura, Hiroshi
PA Ohara Yakuhin Kogyo K. K., Japan
SO Jpn. Kokai Tokkvo Koho, 6 pp.
    CODEN: JKXXAF
DT Patent
   Japanese
LA
FAN.CNT 1
    PATENT NO. KIND DATE APPLICATION NO. DATE
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                                     -----
    -----
                      A √ 20040729 JP 2002-379498
20021227
   JP 2004210660
                                                             20021227
PRAI JP 2002-379498
AB The title compound, Trandolapril benzyl ester, was prepared by reaction of
    (2s, 3aR, 7aS)-hexahydro-2-indolinecarbon acid benzyl ester with N-[1-(S)-
     ethoxycarbonyl-3-phenylpropyl]-L-alanyl-N-carboxy anhydride as an
     antihypertensive agent.
V
    L36 ANSWER 68 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN - CHECKED DOC
AN 2004:490720 CAPLUS Full-text
DN
    141:59698
TI
    ACE inhibitors having antioxidant and NO-donor activity and use for
    cardiovascular, renal and diabetes-associated disorders
IN Haj-Yehia, Abdullah Ibrahim; Khan, Mohamed Amin; Qadri, Bashir Ali
PA Yissum Research Development Company of the Hebrew University of Jerusalem,
    Israel
SO PCT Int. Appl., 91 pp.
    CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
    PATENT NO. KIND DATE APPLICATION NO. DATE
PI WO 2004050084 A2 20040617 WO 2003-IL1006 20031127 WO 2004050084 A3 20040930
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
            NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
            TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
            BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
            ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
            TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
    AU 2003286389
                         A1
                               20040623 AU 2003-286389
                                                                  20031127
                                          EP 2003-777134
    EP 1578413
                         A2
                               20050928
                                                                  20031127
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
    US 20060166894
                        A1
                               20060727
                                          US 2005-536628
PRAI US 2002-429864P
                         P
                               20021129
    US 2002-430003P
                         P
                               20021129
    WO 2003-IL1006
                         W
                               20031127
os
    MARPAT 141:59698
```

The present invention provides multifunctional ACE inhibitor compds. that combine ACE-inhibiting activity with capability to scavenge superoxide and other reactive oxygen species, and that may further function as nitric oxide (NO) donors. The compds. are useful for preventing or treating various disorders, including cardiovascular, and diabetes-associated disorders. This invention is further directed to a method for treating and preventing a disorder in which treatment with an ACE inhibitor is indicated, and mainly cardiovascular disorders, renal disorders, and diabetes-associated disorders. The use of said compds. in the preparation of a medicament is further provided.

√ L36 ANSWER 69 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
TI √ Preparation of aroylhydroxypyrazoles for treatment of metabolic disorders

disorders

√ L36 ANSWER 69 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

Fig. 4. The property of the p

AB

V

in

V L36 ANSWER 70 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN TI V Preparation of N-phenyl or N-heterocyclyldibenzylamine compounds as inhibitors of cholesteryl ester transfer protein (CETP) and medicinal use thereof

L36 ANSWER 71 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN $\sqrt{}$ Method of preparing amine stereoisomers via reduction of sulfinylimines presence of chiral auxiliaries

V L36 ANSWER 72 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

V Preparation of (4-(1,1'-biphenyl-2-ylcarbonylamino or benzoylamino)phenyl]acetic acid esters as microsomal triglyceride transfer protein (MTP) inhibitors

√ L36 ANSWER 73 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

TI $\,\,\,\text{MV}\,\,$ ethods of treating or preventing a cardiovascular condition using a cyclooxygenase-1 inhibitor

L36 ANSWER 74 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2003:255129 CAPLUS Full-text

DN 138:271979

- TI Method for producing enalapril and related angiotensin converting enzyme inhibitors
- IN Tien, Mong-Jong; Liu, Yu-Liang
- PA Everlight USA, Inc., USA

SO U.S., 7 pp. CODEN: USXXAM

DT Patent

LA English FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6541635	B1	20030401	US 2002-178369	20020625
PRAI TW 2002-9110639	9 A	20020329		

OS CASREACT 138:271979

AB The invention discloses a method for producing angiotensin converting enzyme inhibitors (S)-PhCHZCH2CH(COZE)-L-Ala-R (NEPA-R) and pharmaceutically-acceptable salts via deprotection of carboxy group-protected derivs. in non-aqueous medium. The product is obtained in high yield with minimal byproduct formation. Thus, NEPA-L-Pro-OSiMe3, prepared by coupling of NEPA-NCA with H-L-Pro-OSiMe3, was stirred with isopropanol at room temperature and treated with maleic acid to afford 8/1% enalapril maleate.

IT 80876-01-3P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of enalapril and related angiotensin converting enzyme inhibitors via deprotection of silyl esters)

RN 80876-01-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S, 3aS, 7aS)- (CA INDEX NAME)

Absolute stereochemistry.

IT 503322-60-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of enalapril and related angiotensin converting enzyme inhibitors via deprotection of silyl esters)

RN 503322-60-9 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, trimethylsilyl ester, (2S, 3aS, 7aS) - (CA INDEX NAME)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

 $\sqrt{}$ L36 ANSWER 75 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN TI $\sqrt{}$ Compositions comprising a polypeptide and an active agent

 $\sqrt{}$ L36 ANSWER 76 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN TI $\sqrt{}$ Preparation of peptides as STAT modulators

$$\underbrace{^{\text{Y1}}_{\text{Y2}}}^{\text{U}} \underbrace{^{\text{X3}}_{\text{Z}}}^{\text{X3}} \underbrace{^{\text{X}-\text{CO}-\text{A2}-\text{A1}-\text{NR1R2}}}_{\text{X1},\text{X2}}$$

$$\begin{array}{c|c} & \circ & \text{Bu-t} \\ & & \text{Ho_2C} \\ & \text{Ho_2C} \\ & & \text{Ho_2C} \\ \end{array}$$

 $\sqrt{}$ L36 ANSWER 77 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN TI $\sqrt{}$ Compositions comprising a polypeptide and an active agent

 $\sqrt{}$ L36 ANSWER 78 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN TI $\sqrt{}$ Preparation of amino acid salts soluble in organic solvents and their use

in dipeptide synthesis

 $\sqrt{}$ L36 ANSWER 79 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN TI $\sqrt{}$ Cobalamin compounds useful as cardiovascular agents and as imaging

L36 ANSWER 80 OF 111 CAPLUS COPYRIGHT 2008 ACS on

STN

agents

2001:880052 CAPLUS Full-text

DN 136:279663

TI Procedure for the synthesis of ACE-inhibitors

AU Coll, Alberto Palomo; Morte, Sonia Serra

CS Centro Genesis para la Investigacion, S. L., Barcelona, 08021, Spain

SO Afinidad (2001), 58(495), 391-393 CODEN: AFINAE; ISSN: 0001-9704

PB Asociacion de Quimicos del Instituto Quimico de Sarria

DT Journal

LA Spanish

OS CASREACT 136:279663

AB A new simple and economic synthesis of Enalapril maleate and Trandolapril sulfate in 85% yield is described.

IT 406218-99-3P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of ACE-inhibitors)

RN 406218-99-3 CAPLUS

NN 400210-3 CATHON

TH-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, sulfate (2:1) (CA INDEX NAME)

CM

CRN 80876-01-3

CMF C24 H34 N2 O5

Absolute stereochemistry.

CM :

CRN 7664-93-9 CMF H2 O4 S

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

 $\sqrt{}$ L36 ANSWER 81 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN TI $\sqrt{}$ STAT4 and STAT6 binding dipeptide derivatives

√ L36 ANSWER 82 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

TI √ Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction

 $\sqrt{}$ L36 ANSWER 83 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN TI $\sqrt{}$ Preparation and effect of Substituted phenoxyacetic acids in

complications
arising from diabetes mellitus

- √ L36 ANSWER 84 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI $\sqrt{}$ Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction
- √ L36 ANSWER 85 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI $\sqrt{}$ Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction

- L36 ANSWER 86 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI V Combination therapy of angiotensin converting enzyme inhibitor and epoxy-steroidal aldosterone antagonist for treatment of cardiovascular disease

L36 ANSWER 87 OF 111 CAPLUS COPYRIGHT 2008 ACS on

STN

V

AN 1999:705055 CAPLUS Full-text

DN 131:322920

TI Process for preparing N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-L-alanine derivatives

IN Yang, Suh-Wan; Chang, Yu-An; Liu, Yu-Liang

KIND

PA Everlight USA, Inc., USA

SO U.S., 6 pp.

CODEN: USXXAM DT Patent

LA English

FAN.CNT 1

FAN.CNT I

PAIL	NI NO.	KIND	DAIL	AFFLICATION NO.	DAIL
	977380	A	19991102	US 1999-251341	19990217
PRAI US 1	999-251341		19990217		

DATE

OS CASREACT 131:322920; MARPAT 131:322920

AB (\$)-Et02CCH(CH2CH2Ph)-Ala-R (I; R are certain cyclic amino acids, e.g., L-proline) or their pharmaceutically acceptable salts were prepared by coupling I (R = OC6H4R1, where R1 is nitro, cyano, sulfite, carboxy, aldehyde, ester, or halo) with an amino acid. Thus, I (R = OC6H4N02-p), formed by esterifying the acid with 4-nitrophenol in the presence of triethylamine and thionyl chloride in dichloromethane, was treated with L-proline to afford I (R = proline residue) (enalapril).

ADDITIONATION NO

DATE

RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of [(ethoxycarbonyl)phenylpropyl]-L-alanine derivs.)

RN 80876-01-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

L36 ANSWER 88 OF 111 CAPLUS COPYRIGHT 2008 ACS on

AN 1998:38475 CAPLUS Full-text

DN 128:61791

TI Method for the production of L-alanine derivatives with an ACE inhibitor

effect IN Palomo Coll, Alberto; Serra Mortes, Sonia

PA KRKA Tovarna Zdravil D. D., Slovenia

SO Ger. Offen., 6 pp. CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19721290	A1	19971211	DE 1997-19721290	19970521
PRAI	SI 1996-169	A	19960522		

OS MARPAT 128:61791

AB Title compds. RICHZCHZCH(CO2Et)NHCH(CH3)COR2 [(I): Rl = alkyl, aryl, heterocycle; R2 = (un)natural α-amino acid], and their pharmaceutically acceptable salts were prepared as ACE-inhibitors (no data). Thus, (S.S)-I (Rl = Ph; R2 = OH) was reacted with I-proline to yield (S,S)-I (Rl = Ph; R2 = L-proline), which was converted to its maleate salt.

IT 87679-37-6P 200423-23-0P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of L-alanine derivs. with an ACE inhibitor effect)

RN 87679-37-6 CAPLUS

N 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 200423-23-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)], 2a, 3aβ, 7aβ]]-, sulfate (9CI) (CA INDEX NAME)

CM

CRN 80876-01-3

Absolute stereochemistry.

CM 2

CRN 7664-93-9 CMF H2 O4 S

IT 80876-01-3P

RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of L-alanine derive, with an ACE inhibitor effect)

RN 80876-01-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

V L36 ANSWER 89 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

Preparation of carboxylic α -N-sulfino cyclic anhydrides as ACE inhibitor intermediates

L36 ANSWER 90 OF 111 CAPLUS COPYRIGHT 2008 ACS on

STN

1992:651183 CAPLUS Full-text

DN 117:251183

OREF 117:43483a,43486a

Stereoselective synthesis of a trans-octahydroindole derivative, precursor of Ttandolapril (RU 44 570), an inhibitor of angiotensin converting enzyme

AU Brion, F.; Marie, C.; Mackiewicz, P.; Roul, J. M.; Buendia, J.

CS Roussel Uclaf, Romainville, 93230, Fr.

SO Tetrahedron Letters (1992), 33(34), 4889-92

CODEN: TELEAY; ISSN: 0040-4039

DT Journal

LA English

CASREACT 117:251183 os

GT

- AB A stereoselective synthesis of the trans-octahydroindole-2-carboxylic acid I a key intermediate in the elaboration of Trandolapril (RU 44 570) (II) was achieved. The optically active starting material used was obtained from mesodi-Me 1,2-cyclohexanedicarboxylate by an enzymic hydrolysis.
 - 87679-37-6P, Trandolapril

RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent) (stereoselective synthesis of)

RM 87679-37-6 CAPLUS

1H-Indole-2-carboxvlic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonvl)-3phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

V

- √ L36 ANSWER 91 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI V Preparation and formulation of [(mercaptoalky1)carbamoy1]benzoates as analgesics and cardiovascular agents
- V L36 ANSWER 92 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI V Preparation of disulfide derivatives of mercaptoacylamino acids as cardiovascular agents
- √ L36 ANSWER 93 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- √ L36 ANSWER 94 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
- TI √ Preparation of carboxyalkyl dipeptides useful as angiotensin-converting enzyme (ACE) inhibitors
 - 36 ANSWER 95 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN
 - I V Ester prodrug derivatives of carboxylic acid drugs
- AB Ester derive. RCO2(CR2)nCONRIR2 [RCO2 = acyloxy residue of a carboxylic acid drug; Rl,R2 = (substituted) alkyl, alkenyl, aryl, aralkyl, or cycloalkyl, or RlNR2 = (substituted) ring optionallyl containing addnl. N, O, or S; n = 1-3] are prodruge of carboxylic acid drugs RCO2H which are highly stable in aqueous solution but highly susceptible to enzymic hydrolysis in vivo. They are less irritating to the mucosa than the parent drugs and may provide improved bioavailability. The plasma concentration of naproxen in rabbits reached a peak of 7.4 μg/mL 100 min after oral administration of naproxen (4.8 mg/kg), compared to a peak value of 8.3 μg/mL 50 min after oral administration of an equivalent amount of naproxen N,N-bis(β-hydroxyethyl)glycolamide ester (I). The half-life for hydrolysis of I in 80% human plasma at 37° and pH 7.4 was 1.3 min. I was prepared by reaction of naproxen and CLCH2CON(CH2CR2CH2OH)2.

L36 ANSWER 96 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

 $\sqrt{}$ TI Neutral metalloendopeptidase inhibitors in the treatment of hypertension,

compositions and kits containing the inhibitors, manufacture of the compositions, compounds of the compositions and their preparation

AB Neutral metalloendopeptidase (NMEP) inhibitor is used alone or combined with an atrial peptide or an angiotensin converting enzyme (ACE) inhibitor for preparation of pharmaceutical compns. for treating hypertension. The compns. are obtained by mixing a NMEP inhibitor, alone or combined with an atrial peptide or ACE inhibitor, with a pharmaceutically acceptable carrier. S-(4-Methylbenzyl)-L-cysteine, Me ester hydrochloride was prepared by adding thionyl chloride dropwise to N-tert-butyloxycarbonyl-S-(4-methylbenzyl)-L-cysteine in MeOR, heating the mixture under reflux for 90 min, cooling to room temperature, and concentrating in vacuo. Rats with induced hypertension were dosed s.c. with N-(N-[L-1-(2,2-dimethyl-1- oxopropoxy)methoxylcarbonyl)-2-phenylethyl)-L-phenylalanine]- β - alanine and 1-[(2S)-3-mercapto-2-methyl-1-oxypropyl]-L-proline in Me cellulose vehicle to give a 1-, 2-, 3-, and 4-h decrease in blood pressure of 14, 19, 19, and 15 mWHg ws. an increase of 14, 11, 11, and 8 with the NCE inhibitor alone and a decrease of 11, 7, 1, and 1 mWHg with the ACE inhibitor alone.

L36 ANSWER 97 OF 111 CAPLUS COPYRIGHT 2008 ACS on

STN

CS

AN 1987:407555 CAPLUS Full-text

DN 107:7555

OREF 107:1399a,1402a

TI Synthesis and structure activity relationships of potent new angiotensin converting enzyme inhibitors containing saturated bicyclic amino acids

AU Blankley, C. J.; Kaltenbronn, J. S.; DeJohn, D. E.; Werner, A.; Bennett, L. R.; Bobowski, G.; Krolls, U.; Johnson, D. R.; Pearlman, W. M.

L. R.; Bobowski, G.; Krolis, U.; Johnson, D. R.; Pearlman, W. M.
Dep. Chem., Warner-Lambert/Parke-Davis Pharm. Res., Ann Arbor, MI, 48105,

USA

Journal of Medicinal Chemistry (1987), 30(6), 992-8

CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

OS CASREACT 107:7555

GI CASREACT 10/:

- AB The synthesis of a series of angiotensin-converting enzyme (ACE) inhibitors containing saturated bicyclic amino acids in place of proline is described. Octahyroindole-2-carboxylic acid, octahydroisoindole-1- carboxylic acid, and octahydro-3-oxoisoindole-1-carboxylic acid can replace proline in both sulfhydryl and nonsulfhydryl compds.; e.g., sulfhydryl compds. I (R = Ac, H; Rl = H, Me) and nonsulfhydryl compds. II (R2 = Et, H) were prepared Many of the compds. were equipotent to captopril and enalapril in both in vitro and in vivo ACE-inhibiting activity. Structure-activity relationships are discussed. Indolarnil II (R2 = Et) has advanced to clin. evaluation.
- IT 80828-34-8P 80876-05-7P 80923-95-1P 108449-50-9P 108449-51-0P 108449-52-1P 108449-53-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and angiotensin converting enzyme-inhibiting activity of) 80828-34-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

RM

- RN 80876-05-7 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1oxopropyljoctahydro-, [2R-[1[S*(S*)], 2α, 3aβ, 7aβ]]- (9CI) (CA INDEX NAME)

RN 80923-95-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbony1)-3phenylpropyl]amino]-1-oxopropyl]octahydro-, [2R-[1[5*(5*)], 2a, 3aB, 7aB]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 108449-50-9 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(S*)], 2a, 3aB, 7aB]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 108449-51-0 CAPLUS

CN IH-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1oxopropyl]octahydro-, [2S-[1[R*(S*)],2a,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

RN 108449-52-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride, [2R-[1[5*(R*)],2a,3aB,7aB]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

HC1

RN 108449-53-2 CAPLUS

CN lH-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1oxopropyl]octahydro-, [2R-[1[S*(R*)], 2a, 3aβ, 7aβ]]- (9CI)
(CA INDEX NAME)

IT 80828-33-7P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT (Reactant or reagent)

(preparation and hydrolysis of)

- RN 80828-33-7 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester, 12S-[1R:(**)]. Z.a. 3aB, 7aB]. (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 80828-32-6P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and saponification and angiotensin converting enzyme-inhibiting $\ensuremath{\mathsf{C}}$

activity of)

- RN 80828-32-6 CAPLUS
- CN IH-Indole-2-carboxylic acid, 1-[(25)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, hydrochloride (1:1), (2S, 3aS, 7aS) (CA INDEX NAME)

Absolute stereochemistry.

HC1

STN

1987:85063 CAPLUS Full-text

106:85063 DN

OREF 106:13977a,13980a

A new method of obtaining N-acylated proline derivatives

Tremul Lozano, Jesus IN

PA Lazlo Internacional S. A., Spain

SO Span., 8 pp. CODEN: SPXXAD

DT Patent LA

Spanish FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI PRAI	ES 549789 ES 1985-549789	A1	19860316 19851210	ES 1985-549789	19851210

- Title derivs, I [R1, R2 = H, alkvl; R1R2 = (CH2)n; n = 3, 4; R3 = alkvl,AB (CH2) mNH2; m = 3, 4; R4 = OH, alkoxy] are prepared by reacting the corresponding acids (NH2-protected as needed) with 1-(2nitrophenylsulfonyloxy)-6-nitrobenzotriazole (II) in the presence of a base, followed by treatment of the resulting intermediates in situ with the corresponding CO2H-protected amino acids and addnl. base, and final deprotection. Thus, a mixture of N-[1(S)-ethoxycarbonyl-3-phenylpropyl]-(S)alanine, II, and Et3N in MeCN was stirred and treated with a solution of benzyl cis-octahydrocyclopenta[b]pyrrole-2(S)-carboxylate and Et3N in MeCN, followed by workup involving catalytic hydrogenation, to give peptide derivative III.
 - 106554-58-9P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, by peptide coupling with benzotriazolyl sulfonate derivative)

106554-58-9 CAPLUS

CN 1H-Indole-2-carboxylic acid, octahydro-1-[2-[[1-[(1-methylethoxy)carbonyl]-3-phenylpropyl]amino]-1-oxopropyl]-, [2S-[1[R*(R*)], 2α , $3\alpha\beta$, 7α .b eta.]]- (9CI) (CA INDEX NAME)

L36 ANSWER 99 OF 111 CAPLUS COPYRIGHT 2008 ACS on

STN

AN 1987:67669 CAPLUS Full-text

DN 106:67669

OREF 106:11147a,11150a

TI Indolapril

IN Linan Castellet, Isidro; Oliver Mir, Monica

PA Farmhispania S. A., Spain; Bioiberica S. A.

SO Span., 13 pp. CODEN: SPXXAD

DT Patent

LA Spanish

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
ΡI	ES 537841	A1	19860116	ES 1984-537841	19841121	
PRAI	ES 1984-537841		19841121			

AB The title compound, useful as an antihypertensive (no data), was prepared An indole-2-carboxylic acid derivative was N-acylated by MeCHBrCOBr and NAHCO3 and the product was treated with (S)-PhCH2CH2CH(NH2)CO2Et and Et3N to give Indolapril.

T 80876-01-3P, Indolapril

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL

(Biological study); PREP (Preparation)

(preparation of, as antihypertensive)

RN 80876-01-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

$$\sqrt{}$$
 L36 ANSWER 100 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN TI $\sqrt{}$ Medicaments and method of treating heart failure

L36 ANSWER 101 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN V

TI Treatment of coronary insufficiency

Henning, Rainer; Urbach, Hansjoerg; Teetz, Volker; Geiger, Rolf; Schoelkens, Bernward

L36 ANSWER 102 OF 111 CAPLUS COPYRIGHT 2008 ACS

on STN AN 1985:560859 CAPLUS Full-text

DN 103:160859

OREF 103:25849a,25852a

N-Alkylated dipeptides and their esters

IN Teetz, Volker; Wissmann, Hans; Urbach, Hansjoerg

PA Hoechst A.-G. , Fed. Rep. Ger.

SO Eur. Pat. Appl., 33 pp. CODEN: EPXXDW

Patent DT

LA German

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI	EP 135182			EP 1984-110678	19940907
PI			19860305		19040907
	EP 135182		19880727		
				LI, LU, NL, SE	
	DE 3333454			DE 1983-3333454	10020016
		T		AT 1984-110678	
	HU 36145		19850818		19840910
		B			13040310
			19850317		19840913
	FI 8403590 FI 80464	R	19900228	11 1904-3390	13040313
	FI 80464	č	19900611		
	CA 1338163	c	19960312	CA 1984-463078	19840913
	DK 8404405				
	DK 164939	В		DR 1301 1103	13010311
	DK 164939	č			
	NO 8403662		19850318	NO 1984-3662	19840914
	NO 167743	В			
	NO 167743	c	19911204		
	AU 8433070			AU 1984-33070	19840914
	AU 576782	B2	19880908		
	JP 60089497	A	19850520	JP 1984-191868	19840914
	JP 07098835	В	19951025		
	ZA 8407257	A	19850529	ZA 1984-7257	19840914
	ES 535917	A1	19851001	ES 1984-535917	19840914
	IL 72947		19890228	IL 1984-72947	19840914
	US 5068351			US 1990-560004	19900727
PRAI	DE 1983-3333454	A	19830916		
	EP 1984-110678	A	19840907		
	US 1984-650715	B1	19840914		
	US 1986-943882	B1	19861219		
	US 1988-178767	B1	19880330		
	US 1989-403919	B1	19890907		
OS	MARPAT 103:160859				
CT					

AB Title compds. R302CCHR4NRSCCCHRINHCH(CO2R2)(CH2)RR [n = 1, 2; R = H, (un)substituted C1-8 aliphatic, C3-9 alicyclic, C6-12 aromatic, C7-14 araliph., or C7-14 alicyclic aliphatic residue, OR6, SR6 [R6 = (un)substituted C1-4 aliphatic, C6-12 aromatic, C7-14 araliphatic, C6-12 aromatic, C7-16 araliphatic, C3-9 alicyclic, C4-13 alicyclic aliphatic, C6-12 aromatic, C7-16 araliph., or heteroarom. residue, amino acid side chain; R2, R3 = H, (un)substituted C1-6 aliphatic, C3-9 alicyclic, C6-12 aromatic, or C7-16 araliph. residue; CHR4NRS = C5-15 heterocyclic mono-, bi-, or tricyclic ring system) were prepared via the condensation of H02CCHRINNCH(CO2R) (C12) RR with R302CCHR4NHR5 in the presence of phosphinic acid anhydrides R7RBF(O)OF(O)RSP10 [R7, R8, R9, R10 = alkyl or aralkyl). Thus, (S, S, S) - azabicyclo[3.3.0]octane II was condensed with (S)-PhCH2CH2CH(CO2Et)-(S)-Ala-OH by ethylmethylphosphinic acid anhydride to Give Containing Et3N to give peptide III (R1 = CH2Rh), which was debenzylated to give III (R1 = H). I

inhibit angiotensin-converting enzyme and can be used as antihypertensives (no \mathtt{data}).

- IT 80828-32-6P 83542-05-6F 98677-37-2P RL: SFN (Synthetic preparation); PREP (Preparation) (preparation of)
- RN 80828-32-6 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, hydrochloride (1:1), (2S, 3aS, 7aS)- (CA INDEX NAME)

Absolute stereochemistry.

BC1

- RN 83542-05-6 CAPLUS
 CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3
 - n in-indoie-z-carpoxyiic acid, i-[z-[[i-(etnoxycarponyi]-sphenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, [2S-[1[R*(R*)],2a,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

- RN 98677-37-3 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S, 3aR, 7aS)- (CA INDEX NAME)

L36 ANSWER 103 OF 111 CAPLUS COPYRIGHT 2008 ACS

on STN

AN 1985:560858 CAPLUS Full-text

DN 103:160858

OREF 103:25849a,25852a

TI N-Alkylated dipeptides and their esters

IN Urbach, Hansjoerg; Henning, Rainer; Wissmann, Hans; Teetz, Volker

PA Hoechst A.-G. , Fed. Rep. Ger.

SO Eur. Pat. Appl., 32 pp. CODEN: EPXXDW

DT Patent

LA German

FAN.CNT 1

		TENT NO.					DATE		PLICATION NO.	DATE
PI	EP EP	135181 135181			A2 A3		19860402	EP	1984-110677	19840907
		135181					19900131			
			BE,	CH,	DE,	FR,	GB, IT,	LI, L	U, NL, SE	
		3333455			A1		19850411	DE	1983-3333455	19830916
	ΑT	49979			T				1984-110677	
	HŲ	36140			A2				1984-3417	19840910
	HŲ	49979 36140 198303			В		19890928			
	FT	8403591			A		19850317	FI	1984-3591	19840913
	FΙ	80275 80275			В		19900131			
	FΙ	80275			С					
	CA	1338162			С				1984-463071	
		8404404			A		19850317		1984-4404	19840914
	DK	166027			В		19930301			
	DK	166027			С		19930712			
	NO	8403663			A		19850318	NO	1984-3663	19840914
	NO	167808			В		19910902			
		167808					19911218			
		8433071			A				1984-33071	19840914
		575585					19880804			
		60089498					19850520		1984-191869	19840914
		07098836					19951025			
		8407259			A		19850529		1984-7259	19840914
		535918					19851001		1984-535918	
		72946					19900429		1984-72946	
		5055591					19911008		1988-173024	19880323
PRAI		1983-3333					19830916			
	EP	1984-110	577		A		19840907			

US 1984-650714 B1 19840914 US 1986-943881 B1 19861219

G1

AB Title compds. R302CCHR4NR5COCHR1NHCH(CO2R2)(CH2)nR [I; n = 1, 2; R = H, (un)substituted C1-8 aliphatic, C3-9 alicyclic, C6-12 aromatic, C7-14 araliph., or C7-14 alicyclic aliphatic residue, OR6, SR6 [R6 = (un)substituted C1-4 aliphatic, C6-12 aromatic, or heteroarom. residue]; R1 = H, (un) substituted C3-9 alicyclic, C4-13 alicyclic aliphatic, C6-12 aromatic, C7-16 araliph., or heteroarom. residue, amino acid side chain; R2, R3 = H, (un) substituted C1-6 aliphatic, C3-9 alicyclic, C6-12 aromatic, or C7-16 araliph. residue; CHR4NR5 = C5-15 heterocyclic mono-, bi-, or tricyclic ring system] were prepared via the condensation of HO2CCHR1NHCH(CO2R2)(CH2)nR with R302CCHR4NHR5 in the presence of an alkanephosphoric acid anhydride. Thus, (S)-Ala-OH by n-propanephosphonic acid anhydride in CH2C12 in the presence of N-ethylmorpholine to give peptide derivative III (R7 = CH2Ph), which was debenzylated to give III (R7 = H) (all-S isomer). I inhibit angiotensinconverting enzyme and can be used as antihypertensives (no data).

IT 83542-65-6P 96677-37-3P
 RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of)

RN 83542-05-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, [2S-[1[R*(R*)], 2α, 3aβ, 7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 98677-37-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(25)-2-[[(15)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (25, 3aR, 7aS) - (CA INDEX NAME)

L36 ANSWER 104 OF 111 CAPLUS COPYRIGHT 2008 ACS

STN on

1985:185278 CAPLUS Full-text

DN 102:185278

OREF 102:29073a,29076a

Phosphate salts of 1-(2-[(1-alkoxycarbonyl-3-aralkyl)amino]-1-

oxoalkvl)octahvdro-1H-indole-2-carboxvlic acids

IN Seamans, Ronald E.; Behnke, Walter E.

PA Warner-Lambert Co. , USA U.S., 5 pp.

CODEN: USXXAM

DT Patent

LA English

FAN. CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO. I	DATE		
PI	US 4490386	A	19841225	US 1982-422499	19820923		
PRAI	US 1982-422499		19820923				
OS	CASREACT 102:185278;	MARPAI	102:185278				

GI

- AB One example of a phosphate salt of acvlated octahydroindolecarboxylic acids I [R = (un) substituted Ph; m = 0-3; R1 = H, alkyl; R2 = H, alkyl, PhCH2], antihypertensives (no data) was prepared. Thus, the S,S-isomer of Et α -[(1carboxyethyl)amino]benzenebutanoate hydrochloride was treated with tert-Bu (1)-octahydro-1H-indole-2-carboxylate in the presence of 1-hydroxytriazole, Et3N, and dicyclohexylcarbodiimide to give the S,S,S-isomer of I (R = Ph, m = 2, R1 = Et, R2 = Me) as the HCl salt (II). Treating II with 85% H3PO4 gave the 1:1 phosphate salt.
- 96022-35-4P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and formation of phosphate salt from)

RN 96022-35-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride (9CI) (CA INDEX NAME)

HC1

IT 96015-97-3P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of) RN 96015-97-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-

phenylpropyl]amino]-1-oxopropyl]octahydro-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 80876-02-4 CMF C24 H34 N2 O5

CM :

CRN 7664-38-2 CMF H3 O4 P



L36 ANSWER 105 OF 111 CAPLUS COPYRIGHT 2008 ACS

on STN

1984:139616 CAPLUS Full-text

DN 100:139616

OREF 100:21335a,21338a

- Derivatives of bicyclic amino acids, agents containing them and their use, as well as bicyclic amino acids as intermediates
- TN Urbach, Hansjoerg; Henning, Rainer; Teetz, Volker; Geiger, Rolf; Becker, Reinhard; Gaul, Holger
- PA Hoechst A .- G. , Fed. Rep. Ger.
- Eur. Pat. Appl., 103 pp. SO
- CODEN: EPXXDW DT Patent
- LA German

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		Million L										
		PAT	TENT :	NO.			KIND		DATE		APPLICATION NO. DATE	
												-
	PI	EP 84164			A2 1983072		0727	EP 1982-112007 1982122	4			
		EP	8416	4			A3		19831012			
		EP	8416	4			B1 19870128			0128		
			R:	ΑT,	BE,	CH,	DE,	FR,	GB,	ΙT,	LI, LU, NL, SE	
		DE	3151	690			A1		1983	0707		9
		DE	3210	701			A1		1983	1006	DE 1982-3210701 1982032	4
		EΡ	1707	75			A1		1986	0212	EP 1985-103730 1982122	4
		ΕP	1707	75			B1		1989	1108		
		EP	1707	75			B2		1994	1012		
			R:	AT,	BE,	CH,	DE,	FR,	GB,	IT,	LI, LU, NL, SE	
		ΑT	2524	4			T		1987	0215	AT 1982-112007 1982122	4
	PRAI	DE	1981	-315	1690		A		1981	1229		
		DE	1982	-321	0701		A		1982	0324		
		EΡ	1982	-1120	007		P		1982	1224		

- CASREACT 100:139616 OS
- GI For diagram(s), see printed CA Issue.
- AB Title compds. I [R = H, C1-6 alkyl, aminoalkyl, C2-6 alkenyl, C5-9 cycloalkyl, C5-9 cycloalkenyl, C5-7 cycloalkyl-C1-4 alkyl, (un)substituted aryl or partially hydrogenated aryl; R1 = H, C1-6 alkyl, C2-6 alkenyl, aryl-C1-4 alkyl; R2 = H, OH; R3 = H; R2R3 = O; R4 = C1-6 alkyl, C2-6 alkenyl, C5-9 cycloalkyl, (un) substituted aryl, indol-3-yl; n = 0, 1, 2] were prepared as antihypertensives due to their ability to inhibit angiotensin-converting enzyme (ACE). Thus, (S)-PhCH2CH2CH(CO2Et)-(S)-Ala- OH was condensed with (d,1)-2β,3aβ,7aβ-octahydroindole-3- carboxylic acid benzyl ester-HCl by DCC/1hydroxybenzotriazole in DMF containing N-ethylmorpholine to give a mixture of the (2S, 3aR, 7aR) - and (2R, 3aS, 7aS) -diastereoisomers of octahydroindole II (R5 = Et, R6 = CH2Ph) (III). (2S,3AR,7aR)-III was debenzylated by hydrogenolysis and then saponified to give (2S, 3aR, 7aR) - II (R5 = R6 = H). (2S, 3AR, 7aS) - II(R5 = R6 = H) inhibited ACE in rats with an ED50 of 800 ug/kg.
- IT 80875-02-4 83601-86-9

RL: RCT (Reactant); RACT (Reactant or reagent)

(angiotensin converting enzyme-inhibiting activity of)

RN 80876-02-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro- (CA INDEX NAME)

RN 83601-86-9 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropy1)amino]-1oxopropy1]octahydro- (CA INDEX NAME)

IT 87679-71-8P 87679-72-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPM (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

- (preparation and angiotensin converting enzyme-inhibiting activity of)
- RN 87679-71-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

RN

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1oxopropyl)octahydro-, [2S-[1[R*(R*)],2a,3aβ,7aa]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

- IT 87679-37-6P 87679-42-3P
 - RL: SPN (Synthetic preparation); PREP (Preparation) (preparation and angiotensin-converting enzyme-inhibiting activity of)
- RN 87679-37-6 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

- RN 87679-42-3 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-{2-[(1-(ethoxycarbonyl)-3phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2a,3aß,7au]]- (9CI) (CA INDEX NAME)

- IT 87679-29-6P
 - RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and de-tert-butylation of)
- RN 87679-29-6 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester, [2S-[[1R*(R*)],2,a,3aa,/aa]]- [9CI) (CA INDEX NAME)

- IT 87679-41-2P 87827-53-0P
- RL: RCT (Reactant); SFN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and hydrogenolysis of)
- RN 87679-41-2 CAPLUS
- CN IH-Indole-2-carboxylic acid, 1-[(25)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S, 3aS, 7aR)- (CA INDEX NAME)

- RN 87827-53-0 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[1]-(ethoxycarbonyl)-3phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, [25-[1[R*(R*)], 2a, 3aa, 7aa]]- (9CI) (CA INDEX NAME)

IT 87725-71-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and saponification of)

RN 87725-71-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride, [25-[1[R*(R*)], 2a, 3au, 7au]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HC1

- RN 87679-28-5 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-{2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, [2R-[1[5*(5*)], 2a, 3aa, 7aa]]- (9CI) (CA INDEX NAME)

- RN 87679-32-1 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1 xopropyl]octahydro-, [2S-[1[R*(R*)], 2a, 3aa, 7aa]]- (9CI)
 (CA INDEX NAME)

- RN 87679-40-1 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2R, 3aR, 7aS) (CA INDEX NAME)

L36 ANSWER 106 OF 111 CAPLUS COPYRIGHT 2008 ACS

on STN

AN 1984:34404 CAPLUS Full-text

DN 100:34404

OREF 100:5335a,5338a

- TI Derivatives of bicyclic amino acids, an agent containing them, their use, and bicyclic amino acids as intermediates
- IN Urbach, Hansjoerg; Henning, Rainer; Teetz, Volker; Geiger, Rolf; Becker, Reinhard
- PA Hoechst A.-G. , Fed. Rep. Ger.
- SO Ger. Offen., 79 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN		NT NO.			KIND			PLICATION NO.	DATE
PI		151690			A1 C A B2	1983070	7 DE	1981-3151690	
	CA 1	341296			С	2001092	25 CA	1982-418453	19821223
	AU 8	291931			A	1983070	7 AU	1982-91931	19821224
	AU 5	59140			B2	1987022	26		
	EP 8	4164			A2	1983072	27 EP	1982-112007	19821224
	EP 8	4164			A3	1983101	.2		
	EP 8	4164			B1	1983072 1983101 1987012	8		
		R: AT,	BE,	CH,	DE,	FR, GB, IT	, LI, L		
	EP 1	70775			A1	1986021	.2 EP	1985-103730	19821224
	EP 1	70775			B1	1989110	8		
	EP 1	70775			B2	1994101	.2		
		R: AT,	BE,	CH,	DE,	FR, GB, IT	, LI, L	U, NL, SE	
	AT 2	5244			T	1987021	.5 AT	1982-112007	19821224
	AT 4	7838			T	1989111	.5 AT	1985-103730	19821224
	FI 8	204474			A	1983063	0 FI	1982-4474	19821227
		0017			В	1989122	29		
	FI 8	0017 8118569			С	1990041	.0		
	JP 5	8118569			A	1983071	.4 JP	1982-227179	19821224 19821227 19821227 19821227 19821227 19821227 19821228
	JP 0	5087504			B	1993121	.6		
	ES 5	18574			A1	1983100)1 ES	1982-518574	19821227
	IL 6	7572			A	1992081	.8 IL	1982-67572	19821227
		205767			A	1983063	0 DK	1982-5767	19821228
	DK 1	70444			B1 A B C A	1995090	4		
	NO 8	204394			A	1983063	0 NO	1982-4394	19821228
		56786			В	1987081	.7		
	NO 1	56786			С	1987112			
	ZA 8	209523			A	1983102		1982-9523	
	HU 2	7438			A2	1983102	28 HU	1982-4177	19821228
		94278			B B	1988012			
	HU 1	94167						1984-4653	
		21740			A1	1984013		1983-521740	19830422
	NO 8	302741			A B	1983063	0 NO	1983-2741	19830727
	NO 1	58799			В	1988072	25		
		58799			C	1988110			
		206478			C A2 A	1986062		1984-461836	19840824
	US 5	008400			A	1991041			19841121
	FI 8	803456			A B C	1988072	21 FI	1988-3456	19880721
		0675			В	1990033	0		
	FI 8	0675			С	1990071	. 0		
	JP 0	1301695			A	1989120)5 JP	1989-7870 1989-7871	19890118
		1301659			A	1989120 1989120 1994011)5 JP	1989-7871	19890118
	JP 0	6004586			В	1994011	.9		

	US 4933361	A	19900612	US 1989-346339	19890428
	US 5101039	A	19920331	US 1990-468567	19900123
	DK 9201199	A	19920928	DK 1992-1199	19920928
	DK 171232	B1	19960805		
PRAI	DE 1981-3151690	A	19811229		
	DE 1982-3210701	A	19820324		
	CA 1982-418453	A3	19821223		
	EP 1982-112007	P	19821224		
	EP 1985-103730	A	19821224		
	FI 1982-4474	A	19821227		
	US 1982-453092	В3	19821227		
	US 1984-673605	A1	19841121		
os	MARPAT 100:34404				
GT					

Согн

- AB Pyrrolecarboxylic acids I [n = 0-2; Rl = H, alkyl (un)substituted by amino, cycloalk(partly) arryl, (un)substituted alkenyl, cycloalk(en)yl, or (partly hydrogenated)aryl, cyclo- or bicyclic heterocyclyl, side-chain of a naturally occurring amino acid; R2 = H, alk(en)yl, arylalkyl; R3 = alk(en)yl, cycloalkyl, (un)substituted aryl; R4 = H, OH; R5 = H, R4R5 = O) and their physiol. tolerable salts, useful as antihypertensives (ED50 40-1080 µg/kg in rats), were prepared N-[1-(S)-Carboxy-3-phenylpropyl]- (S)-alanyl- (25,3aR,7aR)octahydroindole-2-carboxylic acid II was prepared in 9 steps from indole.
- II 67679-41-2P 87827-53-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (preparation and debenzylation of)
 RN 87679-41-2 CAPLUS

II

CN IH-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S, 3aS, 7aR)- (CA INDEX NAME)

RN 87827-53-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, [2S-[1[R*(R*)], 2a, 3aa, 7aa]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 87679-29-6P

RL: RCT (Reactant); SFN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and hydrogenolysis of)

RN 87679-29-6 CAPLUS

CN lH-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester, [2S-[1[R-(R*)],2 α ,3 α 0,7 α 1]- (9CI) (CA INDEX NAME)

- IT 87725-71-1P 87725-72-2F 87725-73-3P
 RL: RCT (Reactant); SFM (Synthetic preparation); PREP
 (Preparation); RRCT (Reactant or reagent)
 (preparation and saponification of)
- RN 87725-71-1 CAPLUS
- CN lH-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride, [28-[1]R*(R*)], 2a.3au, 7au]1- (921) (CA INDEX NAME)

● HCl

- RN 87725-72-2 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[(25)-2-[[(15)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride, (25,38, 7a5)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

HC1

- RN 87725-73-3 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride, [2S-[1[R*(R*)], 2α, 3αβ, 7αω]]- (9CI) (CA INDEX NAME)

HC1

- IT 87679-71-8 87679-72-9
 RL: RCT (Reactant); RACT (Reactant or reagent)
- (preparation as antihypertensive) RN 87679-71-8 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S, 3aR, 7aS)- (CA INDEX NAME)

Absolute stereochemistry.

- RN 87679-72-9 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1oxopropyl]octahydro-, [2S-[1[R*(R*)], 2a, 3aβ, 7aa]]- (9C1)
 (CA INDEX NAME)

- IT 2/6/9-28-5P 8/6/9-32-1P
 RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)
- RN 87679-28-5 CAPLUS
- CN lH-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, [2R-[1]5*(5*)], 2a, 3aa, 7aa]1- (9C1) (CA INDEX NAME)

- RN 87679-32-1 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1oxopropyl)octahydro-, [2S-[1[R*(R*)], 2a, 3aa, 7aa]]- (9C1)
 (CA INDEX NAME)

- IT 87679-36-5P 87679-37-6P 87679-40-1P 87679-42-3P
 - RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (preparation of, as antihypertensive)
- RN 87679-36-5 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-

 $[1[R*(R*)], 2\alpha, 3a\alpha, 7a\alpha]]$ (9CI) (CA INDEX NAME)

Absolute stereochemistry.

- RN 87679-37-6 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

- RN 87679-40-1 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[(25)-2-[[(15)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2R, 3aR, 7aS) (CA INDEX NAME)

- RN 87679-42-3 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-

phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S- $[1[R^*(R^*)], 2\alpha, 3a\beta, 7a\alpha]$]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L36 ANSWER 107 OF 111 CAPLUS COPYRIGHT 2008 ACS

on	STN

AN 1983:143272 CAPLUS Full-text

DN 98:143272

OREF 98:21821a,21824a

DK 157851

TI Substituted acyl derivatives of octahydro-1H-indole-2-carboxylic acids

IN Hoefle, Milton L.; Bobowski, George

PA Warner-Lambert Co. , USA

SO U.S., 11 pp. Cont.-in-part of U.S. Ser. No. 194,307, abandoned. CODEN: USXXAM

DT Patent

LA English

FAN	.CNT	2										
	PA:	PATENT NO.			KIND DATE		AP.	PLICATION NO.	DATE			
PI	US	4350	704			A		1982	0921	US	1981-233940	 19810217
	IL	6229	4			A		1986	0731	IL	1981-62294	19810304
	IL	7104	5			A		1986	0731	IL	1981-71045	19810304
	ZA	8101	493			A		1982	0331	ZA	1981-1493	19810305
	CA	1205	476			A1		1986	0603	CA	1981-372381	19810305
	EP	3723	1			A2		1981	1007	EP	1981-301243	19810324
	EP	3723	1			A3		1982	0428			
	EP	3723	1			B1		1987	0128			
		R:	AT,	BE,	CH,	DE,	FR,	, GB,	IT,	LU, N	L, SE	
	EP	8834	1			A1		1983	0914	EP	1983-101990	19810324
	EP	8834	1			B1		1987	0722			
		R:	AT,	BE,	CH,	DE,	FR,	, GB,	IT,	LI, L	U, NL, SE	
	EP	8834	2			A1		1983	0914	EP	1983-101991	19810324
		R:	AT,								U, NL, SE	
		2524				T		1987	0215	AT	1981-301243 1983-101990	19810324
		2845										19810324
		8100						1981	1003	FI	1981-971	19810330
		7607				В		1988	0531			
	FΙ	7607	2			C		1988	0909			
	AU	8168	939			A		1981	1008	AU	1981-68939	19810331
	AU	5438	61			B2		1985	0509			
	DK	8101	482			A		1981	1003	DK	1981-1482	19810401

19900226

В

	DIZ	157851	С	19900730			
		8101121	A	19811005	NO	1981-1121	19810401
		156609	В	19870713	MO	1961-1121	13010401
		156609	C	19871021			
		500965	A1	19871021	7.0	1981-500965	19810401
		25950	A2	19830829	HU	1981-846	19810401
		183383	В	19840428			
		30000	A2	19840228	HU	1983-1049	19810401
		187880	В	19860228			
		56161372	A	19811211	JP	1981-48512	19810402
		02047480	В	19901019			
		4425355	A	19840110		1981-277794	19810629
		504189	A1	19820616		1981-504189	19810722
		201782	A5	19830810		1981-233893	19811005
		202146	A5	19830831		1981-233892	19811005
		1246893	A3	19860723		1981-3339202	19811005
		1241988	A3	19860630		1982-3498497	19821010
	FΙ	8504743	A	19851129	FΙ	1985-4743	19851129
	FΙ	76560	В	19880729			
	FΙ	76560	C	19881110			
	NO	8600366	A	19811005	NO	1986-366	19860203
	NO	156898	В	19870907			
	NO	156898	C	19871216			
	DK	8800910	A	19880222	DK	1988-910	19880222
	DK	159419	В	19901015			
	DK	159419	C	19910318			
PRAI	US	1980-137106	A2	19800402			
	US	1980-194307	A2	19801006			
	US	1981-233940	A	19810217			
	EP	1981-301243	P	19810324			
	EP	1983-101990	A	19810324			
	FI	1981-971	A	19810330			
	IL	1984-62294	A	19840531			
OS	CAS	SREACT 98:143272					
GI							

R²S (CH₂) nCHR¹CON

AB The antihypertensive title compds. I [R = H, alkyl, R1 = H, alkyl, PhCH2; R2 = H, R3CO (R3 = alkyl, (un) substituted phenyl); and their pharmaceutically acceptable salts; n = 0, 1] were prepared Thus, (±)-Et (2α,3aβ,7aβ)- octahydro-IH-indole-2-carboxylate, prepared by hydrogenation of Et indole-2-carboxylate was treated with AsSCH2CH2COCl to give Et (2α,3aβ,7aβ)-octahydro-1-[3- (acetylthio)propanoyl]-IH-indole-2-carboxylate (II). The angiotensin converting enzyme inhibitory IC50 of II was 3.8 + 106 M.

IT 80828-32-6P 80828-34-8P 80876-93-5P 80876-95-7P

80876-95-72

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and angiotensin converting enzyme inhibition by) 80828-32-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, hydrochloride (1:1), (2S, 3aS, 7aS)- (CA INDEX NAME)

Absolute stereochemistry.

- RN 80828-34-8 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

- RN 80876-03-5 CAPLUS
- CN 18-Indole-2-carboxylic acid, 1-[2-[11-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride, [2R-[1[5*(5*)], 2α, 3aβ, 7aβ]]- (9CI) (CA INDEX NAME)

HC1

RN 80876-05-7 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1oxopropyl)octahydro-, [2R-[1[S*(S*)], 2α, 3aβ, 7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

- IT 89828-33-7P
 RI: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (preparation and hydrolysis of)
- RN 80828-33-7 CAPLUS
- CN lH-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester, [2S-[1[R^(R^*)],2 α ,3 β h,7 β h]]- (9CI) (CA INDEX NAME)

- IT 80876-04-6P
 - RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and partial hydrolysis of)
- RN 80876-04-6 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbony1)-3-phenylpropyl]amino]-1-oxopropyl]oxian/duc-, 1, 1-dimethylethyl ester, [2R-[1[5*(5*)], 2a, 3aB, 7aB]]- (9CI) (CA INDEX NAME)

L36 ANSWER 108 OF 111 CAPLUS COPYRIGHT 2008 ACS

on STN

- AN 1982:616730 CAPLUS Full-text
- DN 97:216730
- OREF 97:36397a,36400a
- TI Carboxyalkyl dipeptides and pharmaceutical compositions containing them
- IN Neustadt, Bernard R.; Gold, Elijah H.; Smith, Elizabeth M.
- PA Schering Corp., USA
- SO Eur. Pat. Appl., 123 pp.
- CODEN: EPXXDW
- DT Patent
- LA English
- FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 50800	A1	19820505	EP 1981-108348	19811015
	EP 50800	B1	19860618		

	EP	50800		B2	19950607			
		R: AT, BE,	CH,	DE,	FR, GB, IT,			
	AT	20469		T	19860715		1981-108348	19811015
	DK	8104625		A	19820424	DK	1981-4625	19811020
	DK	161523		В	19910715			
	DK	161523		C	19911223			
		8103283		A	19820424	FI	1981-3283	19811020
		83222		В	19910228			
		83222		C	19910610			
		8176614		A	19820429	AU	1981-76614	19811020
	ΑU	554362		B2	19860821			
	ZA	8107261		A	19820929	ZA	1981-7261	19811020
		1341206		C	20010320		1981-388336	19811020
	NO	8103546		A	19820426	NO	1981-3546	19811021
	NO	164983		В	19900827			
	NO	164983		C	19901205			
	JP	57112359		A	19820713	JP	1981-168511	19811021
		01032240		В	19890629			
	IL	64085		A	19861231	IL	1981-64085	19811021
	HU	32785		A2	19840928	HU	1981-3078	19811022
	HU	193146		В	19870828			
	US	4587258		A	19860506	US	1984-635390	19840730
	US	4808573		A	19890228	US	1987-29293	19870323
	US	4818749		A	19890404	US	1987-117008	19871104
	US	4831157		A	19890516	US	1988-250300	19880928
	JP	01163197		A	19890627	JP	1988-283542	19881109
PRAI	US	1980-199886		A	19801023			
	US	1981-258484		A	19810428			
	US	1980-201649		A2	19801028			
	EP	1981-108348		A	19811015			
	US	1981-334053		A2	19811223			
	US	1984-635390		A2	19840730			
	WO	1985-US1406		A	19850726			
	US	1986-817639		A3	19860110			
		1987-29293		A2	19870323			
os	MAI	RPAT 97:21673)					

GΙ

AB RCOCRIRZNHCHR3CONR4CR5R7COR6 [R, R6 = OH, (un)substituted alkoxy, alkenyloxy, (un)substituted NH2; R1 = H, (un)substituted alkyl; R2, R7 = H, (un)substituted alkyl; R2, R7 = H, (un)substituted alkyl; R4, R5 = H, (un)substituted alkyl; R4R5 form ring systems] were prepared as antihypertensives and angiotensin-converting enzyme inhibitors (no data). Thus, H-L-Ala-OCH2Ph tosylate was treated with PhCH2CH2COCO2Et and reduced with NaBH3(CN) and then debenzylated by hydrogenolysis to give (S)-PhCH2CH2CH2CH2CCD2Et)-L-Ala-OH. The latter was condensed with cis, syn-

octahydroindole-2(S)-carboxylic acid benzyl ester to give indole I (R8 = CH2Ph), which was debenzylated by hydrogenolysis to give I (R8 = H).

IT 83542-05-6P

RL: RCT (Reactant); SFN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and hydrogenolysis of)

RN 83542-05-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, [2s-[1]R*(R*)].2a,3aB,7aB|1-(9C1) (CA INDEX NAME)

Absolute stereochemistry.

IT 80876-02-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and saponification of)

RN 80876-02-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro (CA INDEX NAME)

RN 80828-34-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

- RN 80876-01-3 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S, 3aS, 7aS)- (CA INDEX NAME)

- RN 80876-02-4 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro- (CA INDEX NAME)

- RN 83542-06-7 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [25-[1[R*(R*)], 2a, 3aβ, 7aβ]]-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CM 2

CRN 64-19-7

CMF C2 H4 O2

RN 83542-08-9 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, [2S-[1[R*(S*)], 2a, 3aβ, 7aβ]]- (9CI) (CA INDEX NAME)

- RN 83601-86-9 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1oxopropyl]octahydro- (CA INDEX NAME)

L36 ANSWER 109 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1982:616716 CAPLUS Full-text

DN 97:216716

OREF 97:36393a,36396a

TI Substituted imino diacids and pharmaceutical preparations containing them

IN Remond, Georges; Laubie, Michel; Vincent, Michel

PA Science Union et Cie., Societe Française de Recherche Medicale, Fr. SO Eur. Pat. Appl., 38 pp.

CODEN: EPXXDW

- DT Patent
- LA French

FAN.CNT 2

	PA:			KIND	DATE	APPLICATION NO.	DATE
ΡI				A1	19820414	EP 1981-401501	19810929
	EP	49658		B1	19840613		
		R: AT, B	E, CH,	DE, F	R, GB, IT,	LU, NL, SE	
						FR 1980-21095	19801002
	FR	2491469		B1	19830513		
	FR	2503155		A2	19821008	FR 1981-6916 IL 1981-63940 AT 1981-401501 FI 1981-3034	19810407
	FR	2503155		B2	19830701		
	IL	63940		A	19850630	IL 1981-63940	19810925
	AT	7910		T	19840615	AT 1981-401501	19810929
	FΙ	8103034		A	19820403	FI 1981-3034	19810930
	E.T	//230		В	18881031		
	FI	77230		C	19890210		
	DK	8104343		A	19820403	DK 1981-4343 NO 1981-3339	19811001
	DK	157011		В	19891030		
	DK	157011		С	19900326		
	NO	8103339		A	19820405	NO 1981-3339	19811001
	NO	160780		В	19890220		
	140	100/00		Ç	19090331		
		8175949				AU 1981-75949	19811001
		542611			19850228		
	HU	28405		A2	19831228		19811001
	HU	185147 1153827 1341196		В	19841228		
	SU	1153827		A3	19850430		
	CA	1341196		С	20010306		
	JP	57091974		A	19820608		19811002
		01032239					
		8106844					
		4508729					
		4565819					
		4616029		A	19861007 19861007 19870217	US 1984-659275	19841010
		4616031		A	19861007	US 1984-659276	19841010
		4644008		A	19870217	US 1984-659274	19841010
	US	4616030		A	19861007	US 1984-679320	19841206

Heterocyclic amino acid derivs. I and II [R = C1-4 alkyl; R1 = H, C1-4 alkyl; AB R2 = alkyl, mono- or dicycloalkylalkyl, phenylalkyl, (CH2)mXCHR3R4 [R3 = H, C1-4 alkyl, C3-6 cycloalkyl; R4 = H, C1-4 alkyl, C3-6 cycloalkyl, alkoxycarbonyl; X = S, NR5 (R5 = H, Ac, CO2CH2Ph), m = 1, 2]; n = 0, 1] were prepared Thus, (S)-phenylalanine was cyclized with H2CO to give (S)isoquinoline (S)-III (R6 = R7 = H), which was esterified with MeOH/SOC12 and then condensed with Boc-L-Ala-OH (Boc = Me3CO2C) by DCC/1-hydroxybenzotriazole to give (S)-III (R6 = Me, R7 = Boc-L-Ala). The latter was saponified and then Boc-deblocked by CF3CO2H to give (S)-III.CF3CO2H (R6 = H, R7 = H-L-Ala), which was treated with MeCOCO2H and then reduced by NaBH3CN to give isoquinoline (2S)-IV. I and II were useful as therapeutic agents due to their ability to inhibit enkephalinase, carboxypolypeptidase, kininase, and angiotensinconverting enzyme (ACE); e.g., the compds. can be used as antihypertensives since they inhibit ACE. 82961-92-0P TT

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)

82961-92-0 CAPLUS

RN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-CN

phenylpropyl]amino]-1-oxopropyl]octahydro-, (2Z)-2-butenedioate (2:1) (CA INDEX NAME)

CM

CRN 80876-02-4

CMF C24 H34 N2 O5

CM 2

CRN 110-16-7 CMF C4 H4 O4

Double bond geometry as shown.



L36 ANSWER 110 OF 111 CAPLUS COPYRIGHT 2008 ACS on STN

1982:492759 CAPLUS Full-text 97:92759

OREF 97:15483a,15486a

Amino acid derivatives, compositions containing them and their use

IN Geiger, Rolf; Teetz, Volker; Urbach, Hansjoerg; Schoelkens, Bernward; Henning, Rainer

PA Hoechst A.-G., Fed. Rep. Ger. Eur. Pat. Appl., 196 pp. SO

CODEN: EPXXDW

DT Patent LA German

FAN.CNT 1											
	PATENT NO.					KIN)	DATE		APPLICATION NO. DATE	
PI	EP	4695	3			A2		1982	0310	EP 1981-106535 19810	822
	EP	4695	3			A3		1982	0505		
	EP	4695	3			B1		1989	1206		
		R:	AT,	BE,	CH,	DE,	FR,	GB,	IT,	LU, NL, SE	
	DE	3032	709			A1		1982	0429	DE 1980-3032709 19800	830
	DE	3118	191			A1		1982	1125	DE 1981-3118191 19810	508
	EP	2785	30			A2		1988	0817	EP 1988-102408 19810	822
	EP	2785	30			A3		1989	0802		
		R:	AT,	BE,	CH,	DE,	FR,	GB,	IT,	LI, LU, NL, SE	
	EP	3281	60			A1		1989	0816	EP 1989-105371 19810	822
	EP	3281	60			B1		1994	0504		
		R:	AT,	BE,	CH,	DE,	FR,	GB,	IT,	LI, LU, NL, SE	
	AT	4841	5			T		1989	1215	AT 1981-106535 19810	822
	AΤ	1053	01			T		1994	0515	AT 1989-105371 19810	822

	FI	8102652	A	19820301	FI	1981-2652	19810827
	FI	90072	В	19930915			
	FI	90072	C	19931227			
	HU	27874	A2	19831128	HU	1981-2478	19810827
	HU	189531	В	19860728			
	DK	8103835	A	19820301	DK	1981-3835	19810828
	DK	169382	B1	19941017			
	NO	8102933	A	19820301	NO	1981-2933	19810828
	AU	8174718	A	19820311	AU	1981-74718	19810828
	AU	544756	B2	19850613			
	z_{A}	8105988	A	19820825	ZA	1981-5988	19810828
	IL	63683	A	19880331	IL	1981-63683	19810828
	JP	01048918	В	19891020	JP	1981-134401	19810828
	US	5158959	A	19921027	US	1983-565900	19831227
	US	5162362	A	19921110	US	1983-565887	19831227
	ES	530715	A5	19850614	ES	1984-530715	19840316
	AU	8779284	A	19880204	AU	1987-79284	19871001
	AU	599151	B2	19900712			
		01125398	A	19890517	JP	1988-209625	19880825
		06078355	B	19941005			
	AU	8936625	A	19891005	AU	1989-36625	19890620
	AU	627741	B2	19920903			
	JP	04217994	A	19920807	JP	1991-77208	19910318
	JP	07121955	В	19951225			
		90069	В	19930915	FI	1991-4555	19910927
	FΙ	90069	C	19931227			
		90532	В	19931115	FI	1991-4554	19910927
		90532	C	19940225			
		5401766	A	19950328	US	1994-208443	19940309
PRAI	DE	1980-3032709	A	19800830			
	DE	1981-3118191	A	19810508			
	EP	1981-106535	P	19810822			
	EP	1989-105371	A	19810822			
		1981-297191	A3	19810828			
		1982-117311	A	19820705			
		1982-117312	A	19820705			
OS	CAS	SREACT 97:92759;	MARPAT	97:92759			
GI							

AB Amino acid derivs. I (X = fused benzene or cyclohexane ring; R, Rl = alkyl, alkenyl, cycloalkyl, cycloalkyl, cycloalkylalkyl, aryl, partially hydrogenated aryl, aralkyl, heterocyclic residue; R2 = H, alkyl, alkenyl, aralkyl; n= 0, 1) were prepared as long-lasting antihypertensives (no data). Thus, tetrahydroisoquinoline II (R3 = R4 = H) was treated with ZC1 (Z = PhCH2O2C) to give II (R3 = H, R4 = Z), which was esterified with Me3COH by DCC in CH2C12 containing 4-(dimethylamino)pyridine to give 97% II (R3 = CM23, R4 =

Z), which was Z-deblocked by hydrogenolysis and then condensed with Z-Ala-OH by DCC/1-hydroxybenzotriazole to give II (R3 = CMe3, R4 = Z-Ala). The latter was Z-deblocked by hydrogenolysis to give II (R = CMe3, R4 = Ala), which condensed with PhCH2CH2COCO2H and was then reduced with NaBH3CN to give isoquinoline III (R5 = CMe3), which was debutylated by CF3CO2H to give III (R5 = H).

IT 82717-98-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and hydrogenolysis of)

RN 82717-98-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester (CA INDEX NAME)

RN 80876-02-4 CAPLUS

N 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3phenylpropyl]amino]-1-oxopropyl]octahydro- (CA INDEX NAME)

RN 82717-98-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-{2-[(1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester (CA INDEX NAME)

L36 ANSWER 111 OF 111 CAPLUS COPYRIGHT 2008 ACS

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AN 1982:122630 CAPLUS <u>Full-text</u>

DN 96:122630

OREF 96:20133a,20136a

- TI Substituted acyl derivatives of octahydro-1H-indole-2-carboxylic acids
- IN Hoefle, Milton Louis; Bobowski, George
- PA Warner-Lambert Co. , USA
- SO Eur. Pat. Appl., 47 pp.
- CODEN: EPXXDW DT Patent
- LA English
- FAN.CNT 2

TAN.ONI Z						
	PATENT NO.	KIND DATE		APPLICATION NO.	DATE	
PI	EP 37231	A2 19:	311007	EP 1981-301243	19810324	
			320428			
	EP 37231		370128			
	R: AT, BE, CH,			NI CE		
				US 1981-233940		
	ZA 8101493	A 19	320331	ZA 1981-1493	19810305	
	EP 88341	A1 19:	330914	EP 1983-101990	19810324	
	EP 88341	B1 19:	370722			
	R: AT, BE, CH,	DE, FR, G	B, IT, LI	, LU, NL, SE		
	EP 88342	A1 19:	330914	EP 1983-101991	19810324	
	R: AT, BE, CH,	DE, FR, G	3, IT, LI	, LU, NL, SE		
	AT 25243	T 19:	370215	AT 1981-301243	19810324	
	AU 8168939	A 19	311008	AU 1981-68939	19810331	
	AU 543861	B2 19:	350509			
	SU 1246893			SU 1981-3339202	19811005	
	SU 1241988			SU 1982-3498497	19821010	
DDAT	US 1980-137106		300402	50 1702 3470477	17021010	
PRAI						
	US 1980-194307		301006			
	US 1981-233940		310217			
	EP 1981-301243	P 19	310324			
OS	MARPAT 96:122630					
GI						

- AB Indolecarboxylates I (R = H, alkyl; Rl = H, alkyl, CH2Ph; R2 = H, COR3 (R3 = alkyl, C4-9N1-201-251-2 heteroaryl, Ph optionally substituted with 1 or 2 F, Cl, Br, alkyl, alkoxy); n = 0, 1], useful antihypertensives, were prepared Et indole-2-carboxylate was hydrogenated and the octahydro ester 2α, 3aβ, 7aβ-II (R4 = H, R5 = E) hydrolyzed to give 2α, 3aβ, 7aβ-II (R4 = R5 = H).HCl. N-Acylating this in pyridine with AcSCH2CHMeCOCl gave 2α, 3aβ, 7aβ-II (R4 = COCHMeCH2SAc, R5 = H) diasteroisomer A which was hydrolyzed with NH3 in MeOH to give 2α, 3aβ, 7aβ-II (R4 = COCHMeCH2SH, R5 = H) diasteroisomer A, which had in vitro IC50 (inhibitory concentration) for angiotensin converting enzyme of 7.0 + 10-9 M.
- IT 80976-01-3 80923-95-1
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (angiotensin converting enzyme inhibitory activity of)
 RN 80876-01-3 CAPLUS
- NN 80876-01-3 CAPLOS

 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

- RN 80923-95-1 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2R-[1[5*(5*)], 2a, 3aB, 7aB]]- (9CI) (CA INDEX NAME)

- IT 80828-34-8P 80876-05-7P
 - RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation and angiotensin converting enzyme inhibitory activity of)
- RN 80828-34-8 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

- RN 80876-05-7 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1oxopropyl]octahydro-, [2R-[1[S*(S*)], 2α, 3aβ, 7aβ]]- (9C1) (CA INDEX NAME)

- IT 80828-33-7P 80876-04-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); RACT (Reactant or reagent)
 (preparation and hydrolysis of)
- RN 80828-33-7 CAPLUS
- CN lH-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester, [25-[1]R*(R*)], 2a, 3aB, 7aB])- (9CI) (CA INDEX NAME)

- RN 80876-04-6 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester, [2R-[1[5*(5*)],2a,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

- IT 80876-02-4P
 - RL: SFM (Synthetic preparation); PREP (Preparation) (preparation of)
- RN 80876-02-4 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro- (CA INDEX NAME)

- IT 80828-32-6P 80876-03-5P RL: SPN (Synthetic preparation); PREP (Preparation) (preparation, saponification and hydrolysis of)
- RN 80828-32-6 CAPLUS
- CN lH-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, hydrochloride (1:1), (2S, 3aS, 7aS) (CA INDEX NAME)

- RN 80876-03-5 CAPLUS
- CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride, [2R-[1[5*(5*)], 2α, 3αβ, 7αβ]]- (9CI) (CA INDEX NAME)

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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	605.91	1621.66
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-88.80	-112.80

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 10:58:51 ON 05 MAY 2008